ARCHIVES OF SURGERY

VOLUME 33 DECEMBER 1936 NUMBER 6

COPYRIGHT, 1936, BY AMERICAN MEDICAL ASSOCIATION

DIFFERENTIAL ANALYSIS OF BILE ACIDS IN HUMAN GALLBLADDER BILE

RALPH COLP, M.D.
AND
HENRY DOUBILET, M.D.
NEW YORK

The acids of human bile consist of a mixture of cholic, desoxycholic, anthropodeoxycholic and lithocholic acids, mainly combined with taurine and amino-acetic acid (glycine), to form the conjugated bile acids. Because there was no simple practical method to determine quantitatively the several bile acids, the reports in this field have generally concerned themselves with analysis of a portion of the bile acids. Thus the method of Schmidt and Dart estimates only the conjugated bile acids, leaving unmeasured the free bile acids, which may be present in large amounts.[1] The various modifications of the Pettenkofer reaction produce more color with cholic acid than with desoxycholic acid, and accordingly, if cholic acid is used as a standard, the tests yield low results for total bile acids. The reaction of Gregory and Pascoe measures cholic acid only, but in the presence of a large proportion of desoxycholic acid it will yield high false results.[2]

As a result of the extensive investigations into the etiology of gallstones, there has been an increasing need for an accurate quantitative method which would also differentiate the various bile acids in human bile. A number of reports have appeared on the analysis of bile acids and cholesterol in human pathologic bile.[3] These investigations show that if the ratio between bile acids and cholesterol falls below a certain figure, there is a tendency for the cholesterol to precipitate. This precipitation can be shown clearly by dialysis.[3a] However, it is evident

From the Surgical Service of Dr. Ralph Colp and the Laboratories of the Mount Sinai Hospital.

1. Andrews, E.; Hrdina, L., and Dostal, L. E.: Etiology of Gallstones: II. Analysis of Duct Bile from Diseased Livers, Arch. Surg. **25**:1081 (Dec.) 1932.

2. Doubilet, H.: Differential Quantitative Analysis of Bile Acids in Bile and in Duodenal Drainage, J. Biol. Chem. **114**:289 (May) 1936.

3. (*a*) Andrews, E.; Schoenheimer, R., and Hrdina, L.: Etiology of Gallstones: I. Chemical Factors and the Rôle of the Gallbladder, Arch. Surg. **25**: 796 (Oct.) 1932. (*b*) Riegel, C.; Ravdin, I. S.; Morrison, P. J., and Potter, M. J.: Studies of Gallbladder Function: Composition of Gallbladder Bile in Pregnancy, J. A. M. A. **105**:1343 (Oct. 26) 1935.

that in these reports the analyses of bile acids are most likely incomplete because of the methods used. Moreover, since the solubility of cholesterol varies with the different types of bile acids present in human bile,[4] it would be of interest to know the relative amount of these different bile acids in each sample. In addition, it is possible that these various bile acids might vary in their proportions in different pathologic conditions involving the liver. A differential analysis might therefore be of some assistance both in investigating the etiology of hepatic diseases and in making a differential diagnosis.

A method for the differential bile acid analysis of human bile has been reported recently.[2] By combining three different methods, human bile can be analyzed for bile acids combined with taurine and with amino-acetic acid, for cholic acid, for desoxycholic acid and for free bile acids. Since anthropodeoxycholic acid and lithocholic acid, which form apparently only a small portion of the total bile acids, cannot be differentiated from desoxycholic acid so far, they are included with desoxycholic acid.

MATERIAL

Bile from the gallbladder of forty-five patients who were operated on for cholecystitis was analyzed for bile acids by means of this method. The bile was aspirated through the fundus of the gallbladder immediately after the peritoneal cavity was opened, and an analysis was carried out on this freshly obtained material. It was difficult to obtain bile from a normal gallbladder, since the peritoneal cavity was opened only in cases in which some viscus draining into the portal system was diseased. Since it was evident that the liver must also be involved to some degree in such cases, the bile was considered to be abnormal. However, bile was obtained from several persons in whom both the gallbladder and the liver were apparently normal. These analyses together with analyses of bile from the gallbladder of patients with carcinoma of the pancreas associated with early biliary obstruction present the nearest approach to the composition of bile from the normal gallbladder.

METHODS

The method for the differential quantitative bile acid analysis consists in brief of the following procedures:[5] In order to determine the conjugated bile acids, from 2 to 5 cc. of bile is precipitated with alcohol, and the method of Schmidt and Dart is used to determine the bile acids conjugated with taurine and with amino-acetic acid. In addition, depending on the concentration of the bile, from 1 to 20 cc. is precipitated with zinc hydroxide, and the clear bile extract is used to determine both the cholic acid (the colorimetric method of Gregory and Pascoe) and the total bile acids (the iron precipitation method). The free bile acids are calculated by the difference between the total bile acids and the conjugated bile acids.

---

4. Spanner, G. O., and Bauman, L.: The Behaviour of Cholesterol and Other Bile Constituents in Solutions of Bile Salts, J. Biol. Chem. **98**:181 (Oct.) 1932.

5. For a detailed description of the method see J. Biol. Chem. **114**:289, 1936.

RESULTS

Analysis of Bile in Cases of Chronic Cholecystis.—Table 1 gives the results of the analysis of twenty-one samples of bile aspirated from the gallbladder at operation for chronic cholecystitis. In all these cases the cystic duct was found to be open. The diagnosis in each case was established by the histologic examination of the wall of the gallbladder. A few facts in each case which might be relevant to the bile acid analysis are also tabulated (e. g., whether the cystic duct is open or closed, the onset of the last attack, the duration of symptoms, the ability of the gallbladder to fill, concentrate and empty, as determined by the test of Graham and Cole, and the history or presence of jaundice).

The different bile acids are tabulated as bile acids conjugated with taurine and amino-acetic acid, total bile acids conjugated, cholic acid, desoxycholic acid and total bile acids. The percentages of cholic acid and free bile acids as compared to the percentage of total bile acids are also included. The total bile acids represent the bile acids after hydrolysis and are so calculated in order to obtain the percentage of free bile acids by subtraction from the conjugated bile acids. Thus, in case 37 the first figure, representing the bile acids conjugated with taurine, is multiplied by 1.26 to give taurocholic acid, and the second figure, representing the bile acids conjugated with amino-acetic acid, by 1.14 to give the results as glycocholic acid. The total bile acids are then calculated as follows:

Taurocholic acid	=	1.33 × 1.26	=	1.67%
Glycocholic acid	=	3.38 × 1.14	=	3.85%
Free bile acids.....			=	2.39%
Total bile acids.....			=	7.91%

Owing to a number of factors, the percentage of total bile acids vary greatly in different cases. Undoubtedly the amount of stasis, as determined by the thickness of the wall of the gallbladder, the presence of adhesions or of a stone at the cystic duct, the presence of cholangeitis or fibrosis of the liver and the history of a recent acute attack are important factors to be considered. Thus, in case 40 a stone in the first valve of Heister of the cystic duct apparently acted as a one way valve and led to an accumulation of highly concentrated bile. In cases 37, 64, 65, 78, 79, 81C and 95, in which the wall of the gallbladder was noted to be thin, the percentage of bile acids tended to average about 6 per cent. On the other hand, although the wall of the gallbladder was thin in cases 39 and 41, an early biliary cirrhosis was noted at operation, and the bile was found to be thin and of light color and to

TABLE 1.—*Analysis of Bile from the Gallbladder in Cases of Chronic Cholecystitis*

No.	Bile Acids Conjugated with: Taurine	Bile Acids Conjugated with: Amino-Acetic Acid	Total Bile Acids Conjugated	Cholic Acid	Desoxycholic Acid	Total Bile Acids*	Cholic Acid, Percentage	Free Bile Acid, Percentage	Duration of Symptoms	Onset of Last Attack	Calculi in Gallbladder	Roentgen Examination of Gallbladder	Comment
37	1.33	3.38	4.71	1.47	5.63	7.10	21	34	2 yr.	2 wk.	One cholesterol stone	.....	Slight jaundice for 2 wk.; thin gallbladder; common duct normal
39	0.40	0.00	0.40	0.25	1.07	1.32	19	70	6 mo.	9 days	1 small stone	No visualization	Cyst of choledochus; cholangeitis; thin-walled gallbladder; stasis
40	4.66	2.75	7.41	3.33	7.02	10.35	32	28	10 days	3 days	1 calcium-covered cholesterol stone	.....	Stone acted as one way valve, causing high concentration of bile
41	0.36	0.00	0.36	0.22	0.35	0.57	38	36	8 mo.	Daily attacks	Few small stones	.....	Thin-walled atonic gallbladder; early biliary cirrhosis
44	1.29	1.09	2.38	0.61	1.81	2.42	25	2	9 yr.	Daily attacks	2 large cholesterol stones	Gallbladder visualized faintly; negative shadows	Histologic section showed slight acute inflammation
47	1.74	2.60	4.34	1.82	4.48	6.30	29	31	5 yr.	12 days	No stones	No visualization	
48	1.16	0.80	1.96	2.20	4.74	6.94	32	73	15 yr.	5 days	None	No visualization	Attacks accompanied by jaundice; distended gallbladder with duodenum adherent
56	1.18	0.00	1.18	1.31	4.89	6.20	21	81	2 yr.	5 days	Several cholesterol stones	.....	Duodenum and colon adherent to gallbladder; acute attack 5 days before operation
63	....	....	....	0.83	1.87	2.70	30	..	6 yr.	9 days	Many faceted stones	No visualization; ring-shaped shadows seen	Ampulla bound down to common bile duct; edge of liver thick and rounded
64	1.05	1.72	2.77	1.58	3.66	5.24	30	47	2 mo.	4 days	1 large cholesterol stone	Gallbladder visualized; empties after fat meal; negative shadow	Thin-walled gallbladder
65	0.76	2.24	3.00	1.37	2.84	4.21	32	28	9 mo.	9 days	10 small stones	No visualization	Thin-walled gallbladder buried in liver; duodenum and colon adherent
78	....	....	....	1.94	4.18	6.12	32	..	6 mo.	5 days	None	.....	Thin-walled gallbladder surrounded by adhesions; tenderness in right upper quadrant
79	1.53	3.99	5.52	1.93	5.43	7.36	26	25	8 mo.	7 days	Small stones, some in cystic duct	Gallbladder visualized; negative shadows seen	Wall of gallbladder thin; few adhesions; attacks accompanied by chills
80	....	....	....	0.45	0.94	1.39	32	..	10 yr.	19 days	Several large stones	No visualization	Slight jaundice at operation; common duct found normal
81B	0.71	0.56	1.27	0.73	1.39	2.12	34	40	15 yr.	14 days	Small stones	No visualization; opaque shadows seen	
81C	2.12	0.80	2.92	1.45	3.00	4.45	32	32	3 yr.	6 days	1 large cholesterol stone	Gallbladder visualized; negative shadows seen	Wall of gallbladder thin
83	1.11	2.12	3.23	1.41	2.16	3.57	39	9	4 mo.	2 days	Small stones in gallbladder and cystic duct	.....	Distended thickened gallbladder surrounded by adhesions
88	1.53	2.64	4.17	1.94	2.80	4.74	41	12	4 yr.	Constant pain	Many stones	No visualization	
89	1.58	1.45	3.03	0.91	2.24	3.15	30	4	8 yr.	6 mo.	Many stones	....	Wall of gallbladder markedly thickened
93	1.17	3.06	4.23	1.33	4.64	5.97	22	29	2 mo.	.....	15 faceted stones	Gallbladder visualized faintly; negative shadows seen	
95	1.37	3.67	5.04	1.99	4.78	6.77	29	28	6 mo.	Daily attacks	12 cholesterol stones	Gallbladder visualized; negative shadows seen	Wall of gallbladder thin; generalized cholesterosis; chills; white blood cells in bile obtained by duodenal drainage
Average	1.30	1.82	3.21	1.38	3.33	4.71	30	34					

contain a low percentage of bile acids. These two cases, illustrating the effect of involvement of the liver on the excretion of bile acids, are given in detail.

CASE 39.—A Negro aged 49 suffered for six months from attacks of severe epigastric pain radiating to the left upper quadrant of the abdomen. Slight bilirubinemia was present (1. mg. per hundred cubic centimeters). At operation, the liver was found to be enlarged, firm and slightly fibrosed. The gallbladder was thin and distended with 80 cc. of light brownish bile and contained one small cholesterol stone. A cyst of the choledochus, 3 inches (7.6 cm.) in diameter, was found. A probe passed through the sphincter of Oddi with ease. Cholecystectomy and choledochostomy were performed. Histologic examination of a biopsy specimen of the liver obtained with punch revealed a marked polymorphonuclear and lymphocytic periportal infiltration. The fistula closed only after one month, during which time the patient suffered from severe asthenia due to loss of bile. The symptoms recurred after the formation of new bilirubin stone in the choledochus as a result of infection and stasis. The condition was finally cured by choledochoduodenal intubation. The tube was passed by rectum after it remained in the common bile duct for one year.

CASE 41.—A woman aged 39 had severe attacks of pain in the region of the gallbladder for eight months. Although jaundice was not noted, the urine became dark with each attack, and on the patient's admission to the hospital bilirubinemia was found (3.5 mg. per hundred cubic centimeters). At operation the liver was found to be somewhat cirrhotic, with rounded edges. The wall of the gallbladder was thin and distended and contained 90 cc. of muddy-looking bile and a few small calculi. The gallbladder was removed and the cystic duct was drained. A biopsy specimen of the liver obtained with a punch revealed a marked polymorphonuclear periportal infiltration. The biliary fistula persisted for five weeks. On injection of iodized poppy-seed oil 40 per cent an apparent complete biliary obstruction was present, although the stools contained some urobilin. At reoperation, neither stone nor other obstruction was found in the choledochus. Biliary drainage continued for four weeks, when the fistula gradually closed. The patient has been well since, except for one attack of pain and vomiting after a nervous spell.

In the cases of chronic cholecystitis studied (table 1) the ratio of cholic acid to total bile acids varied from 19 to 41 per cent, but most of the figures fell close to the average, which was 30 per cent. The proportion of free bile acids to the total bile acids varied to a greater extent, but the average figure was 34 per cent. The percentage of free bile acids was especially high in three of the twenty-one cases of chronic cholecystitis. In case 39, in which the free bile acids were 70 per cent of the total bile acids, early fibrosis of the liver, cholangeitis and stasis of the gallbladder were present. In case 48 there was recent jaundice, which may explain the excessively high percentage of free bile acids. In case 48 operation was performed five days after an attack, which may explain the high percentage of free bile acids. In these three cases, in addition, the conjugated bile acids were calculated wholly as conjugated with taurine. Taurine aminonitrogen, as calculated from

the alcohol-soluble sulfur-containing material, is often found to be higher than the total aminonitrogen. This result is undoubtedly due to the fact that there are present nontaurine sulfur compounds, such as the ethereal sulfates. The total aminonitrogen in such cases is then calculated as derived from taurine. However, it is to be remembered that amino-acetic acid aminonitrogen may actually be present, but masked by the excessively high sulfur content. The conjugated bile acids in table 1 are on the average divided equally into taurine bile acids and amino-acetic acid bile acids. Thus the average figures are 1.39 per cent conjugated with taurine and 1.82 per cent conjugated with amino-acetic acid. But it can be seen that with a few exceptions the more concentrated the bile, i. e., the nearer it approaches normality, the greater is the proportion of bile acids conjugated with amino-acetic acid as compared to the taurine bile acids. Cases 37, 47, 79, 93 and 95 are examples. On the contrary, the more abnormal the bile, the greater the proportion of taurine bile acids. In cases of severe pathologic conditions, such as cases 39, 41 and 56, in which the percentage of conjugated bile acids is very low, no amino-acetic acid bile acids can be detected by the methods used here.

Analysis of Bile in Cases of Acute Cholecystitis.—The results of bile acid analysis of the contents of the gallbladder in twenty cases of acute cholecystitis are summarized in table 2. The percentage of total bile acids in cases of acute cholecystitis as compared to that in cases of chronic cholecystitis was very low, averaging 1.21 per cent, or about one quarter of the average noted in cases of chronic cholecystitis (table 1). In cases of acute cholecystitis the percentage of cholic acid as compared to that of total bile acids was also low, averaging 17 per cent, or about one half of the cholic acid ratio in cases of chronic cholecystitis. The percentage of free bile acids in cases of acute cholecystitis tended to be greater than that in cases of chronic cholecystitis. There is, however, a confusing factor in computing the free bile acids in cases of acute cholecystitis. The conjugated bile acids are determined on the material extracted from bile with a large volume of boiling alcohol. This is done to extract all the proteins, which, if present, would yield aminonitrogen on hydrolysis. In the bile removed from acutely inflamed gallbladders, some unknown nonbile acid material is present, which is soluble in hot alcohol and yields aminonitrogen on hydrolysis. This extraneous nitrogen cannot be separated and is calculated as being derived from the conjugated bile acids. It follows, therefore, that the results which are much too high are false. Cases 34, 68 and 94 are examples in which the bile acids calculated by the method of Schmidt and Dart yield figures much higher than those for the total bile acids actually present. Case 67, one of hydrops in the terminal stage of

development, is an extreme example. No bile acids could be found, but after carefully extracting the material with boiling alcohol, a calculated yield of 0.12 per cent of conjugated bile acids was found. The amount of this nitrogen-yielding material may vary, of course, thus masking the true percentage of free bile acids. But where this material is absent, the percentage of free bile acids is typically very high, as in cases 46, 72, 81, 97, 98, 101 and 123. In case 98 no conjugated bile acids are present.

In cases in which the cystic duct was closed by an impacted stone, the percentage of total bile acids was quite low. In the eight cases tabulated, the average total bile acid content was 0.65 per cent, one half the total average content. The bile acid content was higher in those cases in which the cystic duct was open, probably as a result of the entry of small amounts of hepatic bile. In case 90 the percentage of total bile acids was quite high. The results here might have been due to extremely rapid concentration with cessation of absorption of bile acids as a result of the widespread gangrene. In cases 19, 34 and 72 the inflammation was due to a reflux of pancreatic juice into the gallbladder, resulting in a chemical cholecystitis.[6]

Analysis of Bile from Normal Gallbladders.—No bile was obtainable from a perfectly normal gallbladder by aspiration. However, in two cases (table 3), in one of which the gallbladder was thought to be involved and in the other of which abscess of the liver was suspected, operation revealed an apparently normal liver and biliary tract. In case 32 the patient gave a history of frequent attacks of pain in the right upper quadrant of the abdomen unassociated with icterus. At operation, since nothing abnormal was found, bile was aspirated from the gallbladder by inserting a needle through the liver. In this case the total bile acid content was 7.66 per cent, the cholic acid content was 44 per cent of the total and the free acid content was 20 per cent of the total. In case 52 the patient gave a history of anorexia, high fever and chills; the white blood cell count was 18,000 per cubic millimeter, and there was definite tenderness over the liver. Exploration for an abscess of the liver gave negative results; the liver and biliary tract were apparently normal. Cholecystostomy was performed. The fistula gradually closed. Four weeks after operation, a roentgenogram of the chest finally revealed the first evidences of widespread miliary tuberculosis. Although the total bile acid content was low in this case, the cholic acid content was 51 per cent of the total and the free bile acid content was 20 per cent of the total. Similar ratios were obtained

6. Colp, R.; Gerber, I. E., and Doubilet, H.: Acute Cholecystitis Associated with Pancreatic Reflexes, Ann. Surg. **103**:67 (Jan.) 1936.

TABLE 2.—*Analysis of Bile from the Gallbladder in Cases of Acute Cholecystitis*

Case No.	Bile Acids Conjugated with: Taurine	Bile Acids Conjugated with: Amino-Acetic* Acid	Total Bile Acids Conjugated	Cholic Acid	Desoxycholic Acid	Total Bile Acids	Cholic Acid, Percentage	Free-Bile Acid, Percentage	Duration of Symptoms	Onset of Last Attack	Cystic Duct	Calculi in Gallbladder	Comment
19	0.50	1.07	1.57	0.15	2.27	2.42	31	35	10 wk.	1 day	Open	None	Chemical cholecystitis with gangrene
34	0.23	0.87	1.10	0.14	0.34	0.48	29	..	18 mo.	5 days	Open	Few small cholesterol stones	Chemical cholecystitis; gangrene; fat necrosis
35	0.24	0.70	0.94	0.11	0.93	1.14	14	18	4 yrs.	36 hr.	Open	Few small cholesterol stones	Very acute process
46	0.15	0.12	0.26	0.04	0.81	0.85	5	70	2 mo.	10 days	Open	None	Acute pancreatitis; gallbladder secondarily involved
59	....	....	....	0.006	0.112	0.11	5	..	2 wk.	5 days	Open	4 cholesterol stones	Edema; gangrene; pancreas enlarged and thickened
67	0.11	0.01	0.12	0.00	0.00	0.00	..	..	10 yr.	10 days	Closed	1 large impacted calculus	Gangrenous gallbladder; white bile
68	0.27	0.12	0.39	0.00	0.32	0.32	0	..	16 yr.	7 days	Closed	.....	Slight jaundice; fever; white cell count, 19,800; early hydrops
72	0.23	0.15	0.38	0.11	1.33	1.44	8	73	19 hr.	19 hr.	Open	Small cholesterol stone	Chemical cholecystitis; marked edema
74	0.27	0.00	0.27	0.02	0.30	0.32	7	15	8 mo.	7 days	Closed	1 large impacted stone	Thick mucoid bile
81	0.33	0.00	0.33	0.23	1.34	1.57	14	81	10 mo.	7 days	Closed	Small stones; one in cystic duct	Thick tarry bile; distended gallbladder; acute inflammation
84	0.32	0.00	0.32	0.12	0.35	0.47	24	30	18 yr.	?	Closed	1 large impacted stone	Clinically chronic; pathologic section showed chronic and acute inflammation
90	1.28	5.75	7.03	1.25	7.09	8.34	15	15	18 mo.	4 days	Open	Many small stones	Large areas of gangrene in wall of gallbladder
92	0.53	0.53	1.06	0.45	1.05	1.50	30	29	5 days	5 days	Open	100 tiny stones	Slightly thickened gallbladder with outside adhesions; high fever before operation
94	1.58	0.08	1.66	0.25	1.03	1.28	20	..	.....	5 days	Open	Many small stones	Acute process; high fever; white blood cell count 22,000
97	0.11	0.00	0.11	0.00	0.38	0.38	0	71	13 yr.	6 days	Closed	Many stones; one in cystic duct	Acute inflammation without gangrene; first stage hydrops
98	0.00	0.00	0.00	0.012	0.30	0.04	29	100	3 mo.	7 days	Open	1 small stone in gallbladder; 1 in common bile duct	Gallbladder not inflamed but cholangeitis present
101	0.02	0.00	0.02	0.01	0.07	0.08	13	75	1 yr.	12 days	Open	Many stones	Subacute inflammation of gallbladder; choledochitis
114	0.19	0.05	0.24	0.03	0.30	0.33	9	28	5 days	5 days	Closed	Many stones	Hydrops
118	....	....	....	0.50	0.58	1.08	46	..	5 yr.	24 days	Open	1 large stone	Acute pancreatitis; pancreatic ferments in bile; gallbladder faintly visualized in roentgenogram showing 1 stone
123	0.07	0.69	0.76	0.57	1.38	1.95	30	61	1 yr.	7 days	Closed	.....	Colon and duodenum adherent to gallbladder, 2 shaking chills; fever and jaundice; beginning hydrops
Average				0.20	1.01	1.21	17	50					

in the analyses of bile obtained through fistulas in the common duct after recovery from the operative procedure. These analyses will be reported in a later communication.

Analyses of bile from the gallbladder in cases of early obstruction due to carcinoma of the pancreas (table 3, cases 38, 116, 86 and 122)

TABLE 3.—*Analysis of Bile from Normal Gallbladders*

Case No.	Bile Acids Conjugated with: Taurine	Bile Acids Conjugated with: Amino-Acetic Acid	Total Bile Acids Conjugated	Cholic Acid	Desoxycholic Acid	Total Bile Acids	Cholic Acid, Percentage	Free Bile Acid Percentage	Comment
32	2.65	3.51	6.16	3.33	4.33	7.66	44	20	Attacks of pain in right upper quadrant for 4 yr.; no icterus; biopsy of liver showed normal histologic structure
52	0.99	0.85	1.84	1.20	1.13	2.33	51	20	Anorexia; fever; chills; white cell count, 18,000; tenderness over liver; final diagnosis, miliary tuberculosis
38	3.80	5.06	8.86	4.25	5.50	9.75	44	19	Cancer of pancreas with obstruction; icterus for 3 wk.; bilirubinemia, 1.5 mg. per 100 cc.; 150 cc. of bile in gallbladder
116	2.33	4.49	6.82	6.13	6.89	13.02	46	47	Cancer of pancreas with obstruction; icterus for 7 wk.; bilirubinemia, 18 mg. per 100 cc.; 200 cc. bile in gallbladder
86	1.96	3.63	5.60	3.62	2.53	6.15	59	9	Cancer of pancreas with obstruction; icterus for 2 wk.; bilirubinemia, 7.5 mg. per 100 cc.; 100 cc. of bile in gallbladder
122	0.81	1.85	2.66	1.70	1.40	3.10	55	14	Cancer of pancreas with obstruction; icterus for 2 wk.; bilirubinemia, 10 mg. per 100 cc.; galactose and sodium benzoate tests show impairment of liver function
122A	0.71	0.00	0.71	0.87	1.16	2.03	43	65	Cancer of choledochus; icterus for 10 days; icteric index, 120; incomplete biliary obstruction
55	0.08	0.02	0.10	0.04	0.10	0.14	25	28	Cancer of pancreas with obstruction; icterus for 6 mo.; bilirubinemia, 18 mg. per 100 cc.; first stage white bile; 140 cc. of bile in gallbladder
113	....	....	....	0.008	0.027	0.035	23	..	Cancer of bile ducts with obstruction; icterus for 7 wk.; bilirubinemia, 18 mg. per 100 cc.; greenish-white bile; acute cholangeitis with cholangeitic abscesses

revealed the proportions of cholic acid and of free bile acids to be somewhat similar to those in cases 32 and 52. However, in cases in which there had been long-standing obstruction, as in case 55 (table 3), the cholic acid content was 25 per cent of the total bile acid content. In case 113, in which obstruction was associated with acute cholangeitis,

the bile acids were found to be in very low concentration, 0.035 per cent, while the cholic acid content was 23 per cent of the total bile acid content.

It is of some interest to note the huge amount of bile salts that may accumulate in the gallbladder during the height of stasis in cases of carcinoma of the pancreas. In case 116, after inclusion of the weight of the conjugated taurine and amino-acetic acid, the percentage of total bile acids was found to be 14.94. Since 200 cc. of bile was present, the gallbladder contained nearly 30 Gm. of bile acids.

In case 52 analysis of bile from a fistula in the gallbladder was of interest, since the gallbladder was undoubtedly irritated and inflamed by the presence of the drainage tube. The results are summarized in table 4. It can be easily seen that the greater the concentration of bile

TABLE 4.—*Analysis of Bile Drained During Cholecystostomy*

Case No.	Day After Operation	Bile Acids Conjugated with: Taurine	Bile Acids Conjugated with: Amino-Acetic Acid	Total Bile Acids Conjugated	Cholic Acid	Desoxycholic Acid	Total Bile Acids	Cholic Acid, Percentage	Free Bile Acid, Percentage
52	Operation	1.00	0.85	1.85	1.20	1.13	2.23	51	20
	2d day	0.37	0.16	0.53	0.19	0.98	1.17	17	53
	5th day	0.35	0.06	0.41	0.21	0.41	0.62	34	34
	8th day	0.27	0.08	0.35	0.19	0.40	0.59	32	41
	15th day	0.22	0.33	0.55	0.20	0.52	0.72	28	24
	19th day	0.26	0.20	0.46	0.14	0.72	0.86	16	46
111	5th day								
	Fistula in gallbladder	0.36	0.02	0.38	0.01	0.01	0.02	50	..
	Choledochal fistula	0.15	0.15	0.30	0.16	0.14	0.30	54	0

acids, the lower is the percentage of cholic acid as compared to the total. The bile from the gallbladder at operation apparently contained bile acids in their normal proportions, but on the second day after operation the cholic acid content fell to 17 per cent of the total bile acid content and the free bile acid content rose to 55 per cent of the total. On the fifth and eighth days, the first reaction to the operation began to subside, and the percentage of cholic acid rose to 34. On the nineteenth day, the concentrative ability of the gallbladder increased, but the percentage of cholic acid fell to 16, while the percentage of free bile acids rose to 46.

In case 111 the gallbladder and common bile duct were drained by separate tubes. The remarkable ability of the inflamed gallbladder to absorb bile acids was clearly demonstrated. Although the bile from the cholecystostomy tube was much more concentrated and darker than the bile drained from the common duct during the same period, the concentration of bile acid had diminished 93 per cent in passing through the inflamed gallbladder. In addition, it can be noted that, as in other

cases of acute cholecystitis, an abnormal material was present in the bile drained from the gallbladder, which yielded a high false figure for the conjugated bile acids.

COMMENT

In analyzing the figures presented here, two important facts are apparent. The first is that no reliance can be placed on any one method of analysis. The second is that in cases of chronic cholecystitis the ratio of the cholic acid and of the free bile acid content to the total bile acid content varies markedly and consistently as compared to that found in cases of acute cholecystitis.

It is apparent that analysis of bile acids by the method of Schmidt and Dart would yield definitely false results in most instances. Even in bile from the apparently normal gallbladder there seems to be about 20 per cent free bile acids, while in cases of acute cholecystitis as high as 100 per cent of the bile acids may be found to be free. In addition, the opposite extreme may also be present, in that the method of Schmidt and Dart will often yield inordinately high false results in pathologic bile. It would seem, therefore, that analyses based on this method are untrustworthy.

The various modifications of the method of Gregory and Pascoe are specific for cholic acid only. Therefore, in human bile especially, in which desoxycholic acid is present in large proportions, this method yields manifestly false results, probably less than half the total bile acids being analyzed. There is a compensatory effect, however, since the presence of a large proportion of desoxycholic acid produces a fine precipitate during the reaction and results in a higher reading for cholic acid than is actually present.[2] There can be no doubt, therefore, that all analyses of human bile based on the method of Gregory and Pascoe are unreliable.

The procedure of Aldrich and Bledsoe, based on the Pettenkofer reaction, probably yields better results in that desoxycholic acid present in human bile takes a slight part in the reaction. Unfortunately, it has been shown that desoxycholic acid produces only about one half to two thirds of the amount of color yielded by cholic acid. It might be argued that by this method as well as by the method of Gregory and Pascoe, the analyses would be relatively correct in comparing different pathologic conditions. It is evident, however, that since the ratio of cholic acid to desoxycholic acid varies tremendously, analyses based on these methods would be incorrect, even relatively.

It is obvious that the significant feature in the analyses presented herein is the marked variations in the proportions of the individual bile acids in each sample. It is, of course, impossible to make any conclusive comparisons between analyses of bile from normal gallblad-

ders and from gallbladders in cases of chronic cholecystitis owing to the lack of normal controls. It would seem, however, that the ratio of cholic acid to total bile acids is much lower in cases of chronic cholecystitis than in cases in which the gallbladder was found to be normal (table 3). Thus the average percentage of cholic acid is 50 in cases 32, 52, 38, 116, 86, 122 and 122A.

In comparing the analyses of bile from the gallbladder in cases of chronic and of acute cholecystitis, the differences are very definite. Aside from the marked reduction in the percentage of total bile acids in cases of acute cholecystitis noted by other investigators,[7] which is due to absorption by the inflamed wall of the gallbladder, it can be seen that various bile acids disappear at different rates. Since the different bile acids vary greatly in their physical properties, such a result should not be unexpected. From the analyses it appears that the bile acids conjugated with amino-acetic acid are more readily absorbed than the taurine-conjugated bile salts. Cholic acid is more readily absorbed than desoxycholic acid, and the conjugated bile acids disappear more quickly than the free bile acids, leaving the latter in preponderance. Stasis of long duration unaccompanied by infection, as in cases 122 and 55 in table 3, apparently leads to this relative resorption of bile acids. It would appear, therefore, that a differential bile acid analysis of bile from the gallbladder should yield results which would be an index not only of the degree of stasis but more especially of the amount of resorption of bile acids due to inflammation of the wall of the gallbladder.

One other point might be noted. In cases 39 and 41, in which analysis revealed rather extreme changes in the ratio of the different bile acids, tending to approach those in cases of acute cholecystitis, the wall of the gallbladder was relatively uninvolved. In each case, however, the liver seemed to be the seat of early biliary cirrhosis and showed on histologic examination a marked polymorphonuclear periportal infiltration. It is difficult to determine whether these changes in the composition of bile acid were due to stasis resulting from the gallbladder alone or whether the pathologic changes in the liver were the cause. Andrews, Hrdina and Dostal reported four cases in which abnormal types of bile acids were excreted by the liver.[1] In each of these cases the liver was apparently the seat of an early biliary cirrhosis. It appears likely, therefore, that the changes noted in the bile acids in cases 39 and 41 are the result of dysfunction of the liver.

---

7. Rosenthal, F., and Licht, H.: Die Resorption der Gallensäuren in der normalen und entzündeten Gallenblase, Klin. Wchnschr. **7**:1952, 1928. Andrews, Schoenheimer and Hrdina.[3a]

CONCLUSIONS

In a number of cases in which the gallbladder was found to be normal, analysis of the bile from the gallbladder revealed the bile acids to consist of about 50 per cent cholic acid and 50 per cent noncholic bile acids, mostly desoxycholic acid. The bile acids were conjugated to the extent of about 80 per cent, half with taurine and half with amino-acetic acid.

In cases of chronic cholecystitis cholic acid formed about one third of the total bile acid content in the bile from the gallbladder. In cases of acute cholecystitis only about one sixth of the total bile acid content was cholic acid.

Free bile acids formed about one third of the total bile acid content in cases of chronic cholecystitits and one half in cases of acute cholecystitis.

Bile acids are absorbed rapidly by the inflamed wall of the gallbladder. This increased permeability is selective, the cholic acid being absorbed more readily than the desoxycholic acid, the bile acids conjugated with amino-acetic acid more quickly than those conjugated with taurine and the conjugated bile acids more readily than the free bile acids.

The fall in the relative percentage of cholic acid and the rise in the relative percentage of free bile acids apparently indicate that absorption of bile acids has taken place.

In two cases in which a pathologic condition of the liver was present, analysis of the bile from the gallbladder revealed the proportions of the various bile acids to be similar to those found in the bile in cases of acute cholecystitis.

OSSIFICATION

THE INFLUENCE OF THE MINERAL CONSTITUENTS OF BONE

J. DEWEY BISGARD, M.D.
OMAHA

To explain the process by which bone is formed two theories have long existed, the chemical, or humoral, theory and the cellular, or vital, theory. These theories diverge principally in respect to whether or not osteoblasts take a part, secretory or otherwise, in the synthesis of the mineral elements into bone. Exponents of both views agree, obviously, that ossification can take place only in the presence of an adequate supply of calcium and of the other constituents of bone, but whether the process can be initiated, hastened or otherwise favorably influenced by a local supply in excess of normal and whether synthetic bone salts introduced into the site of ossification can be utilized by the organism are controversial subjects with which this report of investigation is concerned.

From a study of much clinical and experimental material, Leriche and Policard,[1] early advocates of the chemical theory, were led to sider: . . . "a local calcific surcharge as the determinant of osteogenesis in a suitable fibrous medium." They expressed the belief that the supply of calcium used in the repair of a bone is liberated locally from the bone, which is undergoing repair. This theory led to the assumption on the part of many investigators that reparative ossification failed in certain instances owing to an actual deficiency in available calcium at the site of repair.

Murray,[2] who has stimulated a renewed interest in this subject, has presented much evidence, though inconclusive, that the repair of bone defects in animals and the repair of fractures in man are favorably influenced by saturating the site with the synthetic salts of bone, calcium carbonate, $CaCO_3$, and calcium phosphate, $Ca_3(PO_4)_2$. The favorable results obtained in his clinical cases are subject to the usual criticism of the inability to control all elements entering into the investi-

---

From the Departments of Surgery and Physiology, University of Nebraska, College of Medicine.

1. Leriche, R., and Policard, A.: The Normal and Pathological Physiology of Bone, translated by S. Moore and J. A. Key, St. Louis, C. V. Mosby Company, 1928.

2. Murray, C. R.: Delayed and Non-Union in Fractures in the Adult, Ann. Surg. **93**:961, 1931; scientific exhibits presented at the Seventy-Ninth and Eightieth Annual Sessions of the American Medical Association, 1928 and 1929.

gation, such as the influence exerted by the operative exposure necessary for the introduction of the salts. Using the same salts in a series of experiments on animals similar to those carried out by Murray, Stewart [3] obtained no positive evidence that these salts had a favorable influence on the repair of bone. He concluded that "lime salts and boiled bone, when placed into a bone defect with either traumatized muscle or fascia, do not serve as a source of available calcium resulting in super-saturation of connective tissue and regeneration of missing bone."

Key [4] carried out a similar group of experiments in which large total gaps in the radii of dogs from block resections were filled with calcium carbonate and calcium phosphate in one series and in another with bone powder (bone from which the organic material had been extracted with sodium hydroxide). From the results he concluded that "neither calcium phosphate and carbonate in the proportions in which they occur in bone, nor bone powder, made by the removal of the organic material from bone, appear to stimulate osteogenesis of bone when implanted in a bone defect." Eden [5] found that calcium alone injected at the site of a fracture in both man and animals had no stimulating effect on repair, but that phosphates introduced into a callus hastened ossification.

In respect to ectopic ossification or the formation of bone in tissues which normally do not contain bone, the dependence of ossification on the concentration of calcium in the tissues is more apparent. Such bone has been found in most tissues and in nearly every organ of the body, but in most instances ossification has taken place in degenerated or necrotic tissue which often has previously undergone more or less calcification. There are, no doubt, other contributing factors, such as the presence of cells possessing osteogenic function, and that such a function is possessed by cells other than osteoblasts, notably the epithelium lining the urinary tract, seems fairly well established by the results of such investigations as those carried out by Neuhof [6] and later by Huggins.[7] However, the importance of calcium in initiating

3. Stewart, W. J.: Experimental Bone Regeneration (Using Lime Salts and Autogenous Grafts as Sources of Available Calcium), Surg., Gynec. & Obst. **59**:867, 1934.

4. Key, J. A.: Effect of a Local Calcium Depot on Osteogenesis and Healing of Fractures, J. Bone & Joint Surg. **16**:176, 1934.

5. Eden, R.: Experiments on the Process of Ossification and Methods for Influencing It, Arch. f. klin. Chir. **126**:418, 1923.

6. Neuhof, H.: Fascia Transplantation into Viscera Defects, Surg., Gynec. & Obst. **204**:383, 1917.

7. Huggins, C. B.: The Formation of Bone Under the Influence of Epithelium of the Urinary Tract, Arch. Surg. **22**:377 (March) 1931.

ossification has been demonstrated repeatedly. Annovazzi,[8] Nagelotte,[9] Polettini,[10] Andrei[11] and others have injected calcium into various tissues of animals and some weeks later have recovered from the ears of rabbits and from the tendons of dogs small pieces of bone which have developed at the site of injection. Other substances injected into these same tissues failed to produce bone.

EXPERIMENTAL PROCEDURE

To investigate this problem under circumstances which permitted more accurate control of the elements involved, the following method of procedure was used. Autogenous transplants of certain tissues, as subsequently enumerated in detail, were made to the anterior chamber of each eye of one hundred and fourteen rabbits and three dogs. Immediately after removal from the donor tissue, the transplants were placed into large needles containing tighty fitted stilets. The needles were forced through the cornea at the limbus into the anterior chamber, and the graft was forced out of the needle into the chamber with the stilets. In most instances the grafts promptly became attached to the iris, from which they became vascularized (figs. 1 and 2). After this had taken place and the inflammatory reaction incident to the trauma of operation had subsided, usually within ten days, aqueous suspensions of either bone salts or bone ash were injected through very fine needles into the anterior chambers of approximately half of the eyes. The salts were those which have been found by analyses to be contained in bone and in the proportions found in bone; namely, calcium phosphate, 85 per cent; calcium carbonate, 14 per cent, and magnesium phosphate, 1 per cent.[12] In many instances the injections were repeated so as to keep the transplants, which usually became attached to the iris at the bottom of the eye, bathed constantly for several weeks in salts or ash (fig. 3). The transplants in the eyes into which salts were not injected served as controls. Utilization of the anterior chamber of the eye for a culture medium has been used by several investigators, among them Polacco,[13] Podleschka and Dworzak[14] and Allan and Priest.[15] It offers certain advantages

8. Annovazzi, G.: Experimental Production of Bone by Injection of Calcium Salts, Arch. ital. di chir. **23**:537, 1929.

9. Nagelotte, J.: Ostéogénèse dans les greffes de cartilage mort, Compt. rend. Acad. d. sc. **169**:737, 1919.

10. Polettini, B.: Ulteriore contributo allo studio de neoformazioni ossee e cartilaginee determinate da innesti de tessuti fissati, Arch. ital. di chir. **7**:169, 1923.

11. Andrei, O.: Sulla produzione di osso e di cartilagine in seguito ad innesti de tessuit fissati e viventi, Arch. ital. di chir. **11**:483, 1925.

12. Wells, H. G.: Chemical Pathology, ed. 4, Philadelphia, W. B. Saunders Company, 1920.

13. Polacco, E.: Comparative Research Work on Bony Neoformations During Autoplastic Grafting of Periosteum and of Young Bone, Arch. per le sc. med. **53**:476, 1929.

14. Podleschka, K., and Dworzak, H.: Transplantation of Organs into the Anterior Chamber of the Eye of the Rabbit as a Biologic Method, Med. Klin. **30**:438, 1924.

15. Allan, E., and Priest, F. O.: Physiological Response of Ectopic Ovarian and Endometrial Tissue, Surg., Gynec. & Obst. **55**:553, 1932.

in that it is possible to culture tissue in vivo and yet have the culture suspended in a medium which can be altered and controlled to a certain degree. It also provides opportunity to observe the graft as often as one wishes.

After varying periods of time the animals were killed, and the grafts were recovered and studied microscopically.

EXPERIMENT 1.—*Transplants of bone (only) versus bone and bone salts.*

Small fragments of bone were removed subperiosteally from the tibia of each of twenty rabbits and placed into the anterior chambers of the eyes of each animal. From ten to fifteen days later bone salts were injected into fifteen of the eyes. In only nine rabbits did both eyes remain uninfected and normal. Each of these provided a pair of transplants for comparison, one of the pair cultured in a medium saturated with bone salts and the other, as illustrated in figures 1 and 4, in normal aqueous. The first pair of transplants were studied micro-

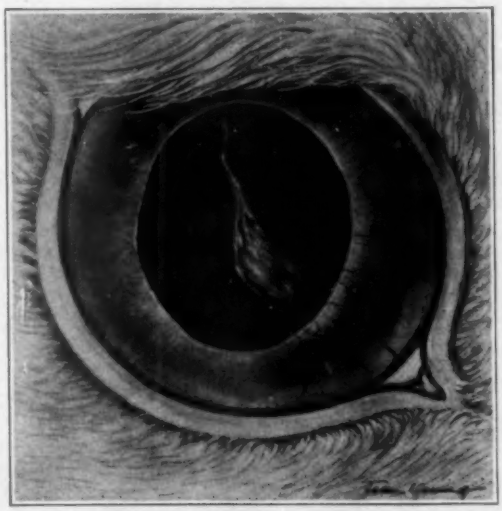

Fig. 1.—Drawing of the right eye of rabbit 14, showing a transplanted segment of bone attached directly to the iris below and by a long pedicle above. Note the blood vessels in the region of attachment of the graft.

scopically eight days and the last pair one hundred and seventy-six days after transplantation and the others at intervals intervening. There were in addition to these, twelve unpaired and uninfected eyes, two containing bone salts. Some of the latter were studied as early as four days after transplantation.

The results may be summarized as follows: The major portion of each transplanted segment of bone became necrotic, but in each specimen there were areas in which the bone cells were alive, particularly the cells near the surfaces. New bone was apparent as early as eight days after transplantation. It appeared first on the surfaces and appeared no earlier and in no greater abundance in the transplants bathed in bone salts.

The necrotic old bone gradually became absorbed and to some extent became replaced by new bone. Absorption first took place on the surface attached to the

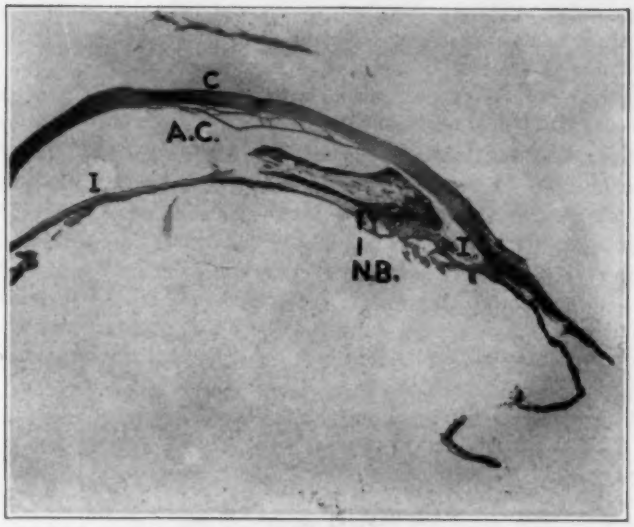

Fig. 2.—Low power photomicrograph of an eye of a rabbit showing an autogenous transplant of periosteum which is attached to the iris, *I*, from which it received its blood supply. It is suspended in the anterior chamber (*A.C.*) and has given rise to much new bone (*N.B.*). The cornea is labeled *C*. This transplant was one hundred and thirty-two days old.

Fig. 3.—Drawing of the right eye of rabbit 32. A segment of periosteum was transplanted into the anterior chamber, and ten days later bone salts were injected in sufficient quantity to saturate the medium about the transplant. Note that the salts almost completely submerge it.

iris and seemed to extend from this area. In the tissue invading the graft there were many pigmented (melanin) cells. Bone salts were found encysted in the iris and in the fibrous tissue attaching it to the graft.

There was no evidence that the bone salts influenced either the fate of the transplant or the formation of new bone.

EXPERIMENT 2.—*Transplants of bone and periosteum versus periosteum (alone).*

Seven rabbits received transplants from their tibias of bone and periosteum in one eye and of periosteum alone in the other eye. Two eyes became grossly infected, leaving twelve transplants but only five pairs. These were sectioned at

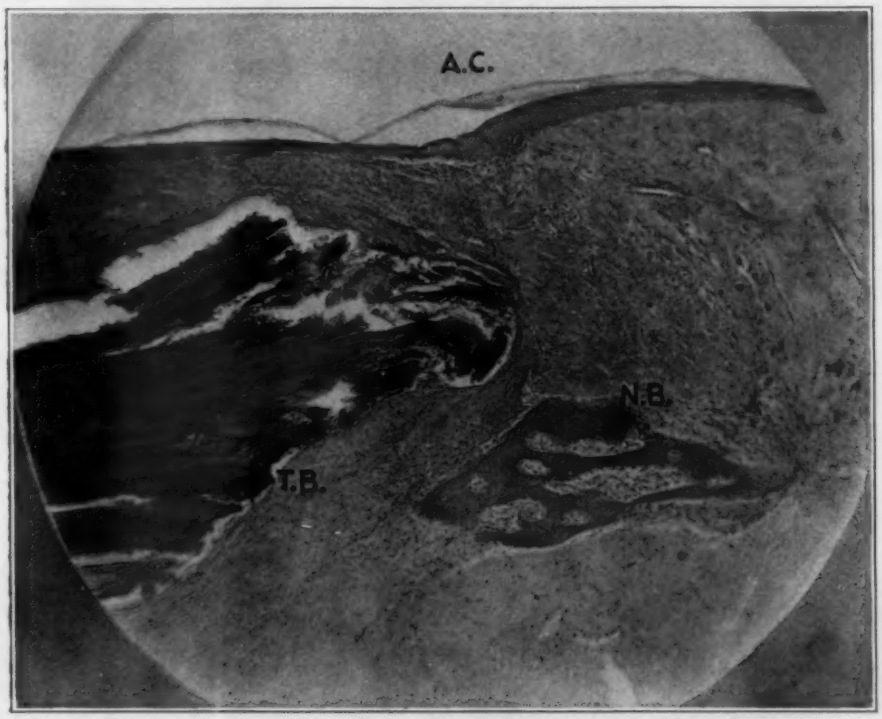

Fig. 4.—A photomicrograph of an autogenous transplanted segment of bone (*T.B.*) in the anterior chamber of an eye of a rabbit. It is surrounded by the fibrous tissue by which it is attached to the iris and cornea. The old bone is partially necrotic and in many areas is undergoing absorption and invasion by granulation tissue. A short distance from the transplant there is a mass of new bone (*N.B.*) consisting of anastomosing trabeculae with fibrous marrow. It is surrounded by a very vascular and cellular zone composed of actively proliferating osteoblastic cells. *A.C.* designates the anterior chamber. The transplant was twenty-one days old.

intervals varying from five to one hundred and twelve days after transplantation. A transplant which supposedly consisted of periosteum alone contained a minute sliver of old bone.

There was new bone arising from the surface of all periosteal transplants with the exception of the one observed at five days. New bone was present in all

specimens containing both bone and periosteum and obviously was much greater in amount and was arising from a much more extensive surface area than was that developing from grafts of periosteum alone. Melanin cells were present in the fibrous tissue invading the graft. Each periosteal transplant contained areas of necrotic tissue. A transplant of periosteum only with an unusually luxuriant growth of new bone is illustrated in figures 2 and 5.

The transplanted segments of bone presented the same histologic picture and succession of changes enumerated in experiment 1.

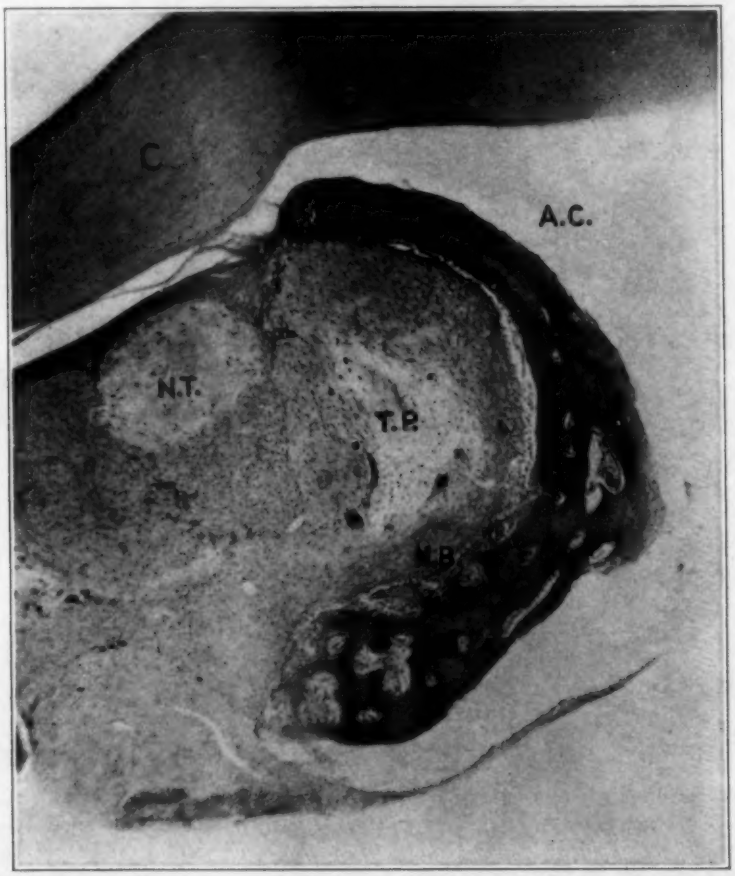

Fig. 5.—Higher power photomicrograph of a portion of the same transplant shown in figure 2. The transplanted segment of periosteum (*T.P.*) contains several areas of necrotic tissue and on its free edge a segment of anastomosing trabeculae of new bone. Designated also are the anterior chamber (*A.C.*) and the cornea (*C.*).

EXPERIMENT 3.—*Transplants of periosteum versus periosteum and bone salts.* Comparative studies were made of thirty-three autogenous transplants of periosteum cultured in the eyes of twenty-one animals. Fifteen had been cultured in an aqueous humor containing bone salts, and the remaining eighteen were controls. New bone was found in twelve of the eighteen controls and in ten of the

fifteen specimens which were bathed in bone salts. New bone was found in specimens of both series when first examined ten days after transplantation, and in these and in specimens cultured at various periods up to one hundred and sixty-one days there was no demonstrable difference in the osteogenic activity or the quantity of newly formed bone. All transplants contained areas of necrotic tissue and pigmented cells, and a few had small encysted collections of salts.

EXPERIMENT 4.—*Transplants of boiled bone.*

In three rabbits autogenous transplants of small bits of bone removed from the tibias and boiled for a few minutes were made to the anterior chambers of each eye. Two eyes became grossly infected. A third transplant became attached to the cornea and apparently failed to establish a communication with vascular tissue, as indicated by the fact that it was entirely necrotic when examined sixty-five days after transplantation.

The other three transplants were attached to the iris and were cultured thirty-eight, sixty and sixty-five days, respectively. Histologic examination showed that all were necrotic but were undergoing absorption and invasion by granulation tissue which contained some pigmented cells, and in each specimen there was new bone in the fibrous tissue by which it was attached to the iris.

EXPERIMENT 5.—*Transplants of fascia versus fascia and bone salts.*

Fascia (autogenous) excised from the sheath of the rectus muscle was transplanted to the anterior chamber of each eye of fourteen rabbits. Into ten of the eyes bone salts were injected approximately ten days later. Microscopic examinations at periods varying from fifteen to one hundred and sixty days were made of eight specimens cultured in an aqueous humor containing bone salts and of thirteen in aqueous humor only.

All transplants were partially necrotic, and four were entirely so, three of them being apparently unattached to any tissue within the anterior chamber. Small particles of bone salts were encysted in the fibrous tissue, attaching the iris to the transplant in three of the specimens, but no specimen contained bone. There were many pigmented cells in the newly formed fibrous tissue.

EXPERIMENT 6.—*Transplants of mucosa of the urinary bladder alone versus the same plus bone salts.*

The urinary bladder was exposed in four rabbits, the serosa and muscularis teased from the mucosa and small pieces of this tissue excised, washed thoroughly in warm physiologic solution of sodium chloride and transplanted to the anterior chamber of each eye. Into three eyes bone salts were subsequently injected. Five specimens, two cultured in bone salts and three controls, were examined, one each at sixty-two days and the others at one hundred and eighty days. All contained epithelium characteristic of that lining the bladder. It was arranged in both single and multiple layers of cells which lined cysts containing a clear fluid stained faintly with eosin. There was also a submucosal layer of areolar tissue. No specimen, however, contained bone.

EXPERIMENT 7.—*Transplants of mucosa of the urinary bladder and fascia of the sheath of the rectus muscle versus the same tissues with the addition of bone salts.*

Eighteen rabbits with transplants of both mucosa of the urinary bladder and of fascia from the sheath of the rectus muscle in the anterior chamber of each eye provided twenty-four satisfactory specimens, eight of which had been cultured in a medium saturated with bone salts. The specimens were examined at periods varying from thirty-two to one hundred and sixty days after transplantation. Much of the fascia in each specimen was necrotic. Epithelium characteristic of

that lining the bladder (apparently very actively proliferating) was present in seven of the eight transplants cultured with bone salts and in fifteen of the sixteen controls. It had the same histologic characteristics as described in the preceding experiment. A photomicrograph of one specimen is illustrated in figure 6.

EXPERIMENT 8.—*Transplants of fascia plus bone ash.*

Bone ash was injected into the anterior chambers of seven eyes to which fascia from the sheath of the rectus muscle had been transplanted from eight to

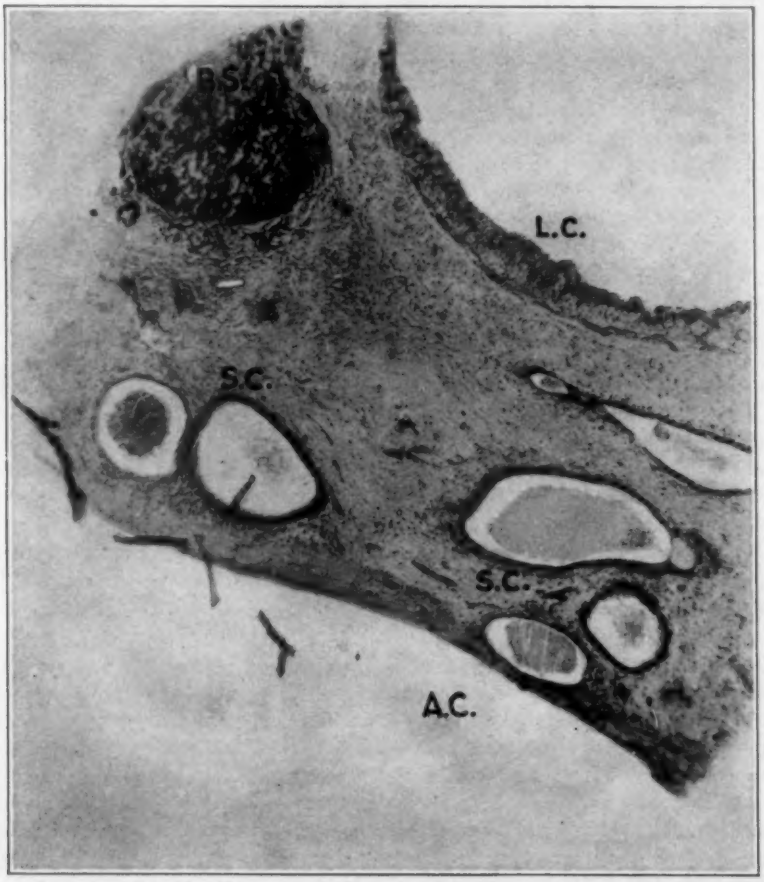

Fig. 6.—Photomicrograph of an autogenous transplant of mucosa of the urinary bladder and of fascia from the sheath of the rectus muscle in the anterior chamber of an eye of a rabbit one hundred and twenty days after transplantation. There is one large cyst (*L.C.*) and several small ones (*S.C.*) which are lined by stratified cuboidal epithelium (bladder) and contain fluid. Into the anterior chamber (*A.C.*) bone salts had been injected twice, some of which became encysted. There is no bone.

twelve days previously. The ash was obtained by baking large segments of the tibias of two rabbits in a furnace. In each instance the ash settled to the bottom of the anterior chamber and partially or completely surrounded the grafts. They were examined after twenty-six, forty-two, sixty-eight, eighty-two, one hundred

and twenty and one hundred and twenty-four days of culture. In each specimen there was much necrotic tissue, but in no specimen was there bone or calcified tissue. The granulation tissue contained many pigmented cells.

EXPERIMENT 9.—*Transplants of mucosa of the urinary bladder and fascia plus bone ash.*

Five transplants from five rabbits consisting of mucosa from the urinary bladder and fascia from the sheath of the rectus muscle were examined thirty-five, forty-eight, seventy, one hundred and twenty-two and one hundred and thirty days after

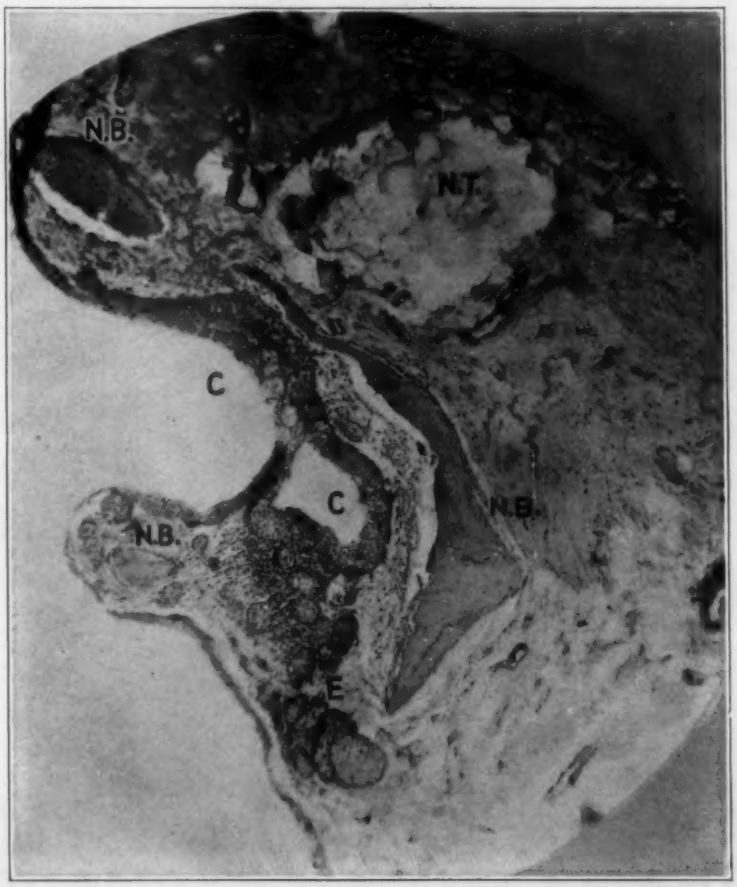

Fig. 7.—Photomicrograph of an autogenous transplant of mucosa of the urinary bladder and of fascia from the sheath of the rectus muscle in the anterior chamber of the eye of a rabbit one hundred and twenty-two days after transplantation. The transplanted tissue had been bathed in bone ash which had been injected into the anterior chamber twelve days after transplantation. As in figure 6, there are cysts lined with epithelium characteristic of that lining the bladder, but there is the important difference of the presence of plaques of new bone (*N.B.*) in the submucosal tissue. There are also solid cords of large epithelial cells (*E.*) and an area of necrotic tissue (*N.T.*).

transplantation. They had been cultured in the anterior chamber in an aqueous humor to which had been added sufficient bone ash to cover them completely.

In four of the five specimens there were many cysts lined with stratified cuboidal epithelium (of the type seen in the bladder) and areas containing these same cells arranged in solid cords. The transplanted fascia was partially necrotic. In two of these transplants, as illustrated in figure 7, there were plaques of new bone in the submucosal areolar tissue of the walls of several cysts, but in each instance it was confined to only a portion of the circumference of the cysts. The bone contained haversian canals and both fibrous and hematopoietic marrow.

Fig. 8.—Photomicrograph of an autogenous transplant of mucosa of the urinary bladder and of fascia from the sheath of the rectus muscle in the anterior chamber of the eye of a dog. Note the cysts (*C.*) lined with epithelium characteristic of that lining the bladder and a mass of new bone (*N.B.*) in the submucosal fibrous tissue of a large cyst. Neither bone salts nor bone ash had been introduced into the eye.

EXPERIMENT 10.—*Transplants of mucosa of the urinary bladder and fascia of the sheath of rectus muscle.*

Transplants of the mucosa of the urinary bladder and fascia of the sheath of the rectus muscle to the eyes of three dogs yielded, seventy-two days after

transplantation, four satisfactory specimens, but only two contained epithelium characteristic of that lining the bladder. In each of these, however, there were epithelium-lined cysts, and in the walls of some of the cysts there were plaques of new bone. This bone contained haversian canals but only fibrous marrow. A photomicrograph of one specimen is illustrated in figure 8.

EXPERIMENT 11.—*Transplants of mucosa of the gallbladder and fascia of the sheath of the rectus muscle versus the same tissues with the addition of bone salts.*

In six rabbits there were placed into the anterior chambers of the eyes autogenous transplants of both mucosa of the gallbladder and of fascia from the sheath of the rectus muscle. Ten days later bone salts were injected into four eyes. The animals were killed thirty-two and seventy-five days later, and eight specimens were obtained for examination, consisting of four which had been cultured in aqueous saturated with bone salts and four controls. Two of the former and three of the latter specimens contained epithelium characteristic of that lining the gallbladder. In each instance the cells lined cysts, which were small and numerous. No specimen, however, contained bone. Much of the fascia was necrotic.

EXPERIMENT 12.—*Control rabbits.*

To determine whether trauma to the eye incident to the operative procedure necessary for the introduction of the transplants or whether the presence of the bone salts in the anterior chamber might in themselves induce osteogenesis in the tissues of the eye, these procedures were carried out, each in six rabbits. The eyes were examined both grossly and in serial microscopic sections at intervals ranging from sixteen to one hundred and seventy-six days. In a few instances bone salts were encysted in the iris, but in no specimen was bone found.

EXPERIMENT 13.—*Infection.*

Not infrequently bone has been found in human eyes in which there has been a panophthalmitis with subsequent recovery from infection and replacement of the necrotic tissue with fibrous tissue. As recorded in the report of the foregoing experiments, several rabbits acquired ophthalmitis in eyes in which the various transplants had been placed. Fourteen of these were carefully examined grossly, and all tissue with the consistency of bone was sectioned and studied microscopically. All had had the original infection more than one hundred and twenty days previously. In no specimen was bone found.

SUMMARY

In this group of experiments the anterior chambers of the eyes served as living culture tubes. In them tissues were cultured with direct vascular communications so that they received not only nutrition but also minerals, hormones, etc. By their vascular attachments they were suspended in a fluid which normally consists almost entirely of water. Its mineral content is negligible. Tissues cultured in this neutral medium served as controls for comparison with identical tissues cultured in aqueous surcharged with either bone salts or bone ash. Since the transplants contained necrotic tissue and were invaded by granulation tissue, there were present all the factors which the proponents of the chemical theory consider adequate for ossification, namely, a local surcharge of calcium, an active blood supply and fibroblasts.

Tissues known to be osteogenic, such as bone and periosteum, gave rise in each instance to new bone, and in comparing the control specimens with those cultured in bone salts no difference could be demonstrated in respect to the time of the beginning of ossification or in respect to the quantity or quality of the new bone. A much more luxuriant growth of bone formed from periosteum with which bone also had been transplanted than from transplants of periosteum alone.

Contrary to the observations of Key,[4] bone devitalized by boiling was found not to be inert. In the anterior chamber it gave rise to the formation of new bone in the surrounding fibrous tissue.

Fibrous tissue such as that present in the sheath of the rectus muscle failed to either calcify or ossify, regardless of the calcium content of the aqueous humor in which it was cultured.

It has been shown by Huggins[7] that the epithelium lining the urinary tract cultured in contact with certain types of fibrous tissue in vivo causes the deposition of bone in this fibrous tissue. Utilizing this contribution for the purposes of this problem, transplants consisting of epithelium from the bladder and fascia of the sheath of the rectus muscle were made into the anterior chambers of the eyes of both dogs and rabbits. In the dogs bone constantly developed in the submucosal fibrous tissue of the epithelial-lined cysts. None of the eyes of the dogs received bone salts. The same type of transplants in the rabbit cultured both with and without bone salts failed in each instance to produce bone. There developed only cysts lined with cuboidal epithelium. This distinction of behavior of transplanted epithelium from the bladder in the two types of animals was also observed by Huggins.[7]

However, in two of four transplants in rabbits in which the epithelium and fascia were cultured in mediums of aqueous containing bone ash, bone was deposited as in dogs in the fibrous tissue adjacent to the epithelium, which in many areas circumscribed fluid-filled cysts.

No bone was found in three series of eyes used as controls, namely, those into which bone salts only were injected, those subjected to operative trauma only and those in which infection had caused extensive destruction and fibrosis of the interior of the eyes. Only the latter group contained grafts.

CONCLUSIONS

The results of this investigation indicates that in experimental animals:

1. The synthetic salts of bone, calcium carbonate, $CaCO_3$, calcium phosphate, $Ca_3(PO_4)_2$, and magnesium phosphate, $Mg_3(PO_4)_2$, have no influence on osteogenesis or ossification. In great concentration and in the presence of tissue not in itself osteogenic but recognized as

ossifiable, these salts failed to give rise to the formation of bone, and in the presence of osteogenic tissue they appeared not to alter the normal course of ossification.

2. Bone, regardless of its viability, has a favorable influence on ossification. This was true of partially viable bone, boiled bone and bone ash. Transplants of the former invariably initiated ossification in the fibrous tissue surrounding them. This was also true of boiled bone, but to a much lesser degree, and although it did not occur with the use of bone ash under similar circumstances ossification did take place in transplants of fibrous tissue and epithelium from the bladder which were bathed in bone ash. Since bone was not formed in this type of transplant in the rabbit in mediums of either normal aqueous or bone salts, it is deduced that bone ash possesses some factor favorable to ossification which is not present in bone salts. It would seem likely, as suggested by Watt,[16] that calcium as it exists in bone exists in a physiochemical or structural form more suitable for use in the process of ossification.

---

16. Watt, J. C.: The Deposition of Calcium Phosphate and Calcium Carbonate in Bone and in Areas of Calcification, Arch. Surg. **10**:983 (May) 1925.

A PLAN FOR THE TREATMENT OF CANCER WITH SMALL QUANTITIES OF RADIUM

GEORGE T. PACK, M.D.
NEW YORK

A disease such as cancer, which is inevitably fatal if untreated, should receive the best possible management by physicians skilled in its diagnosis and treatment. The cancer institute is the ideal solution, as it includes a hospital organized and maintained solely for the diagnosis and treatment of cancer as well as adequate research laboratories. It is not feasible to care for all patients with cancer in institutes or hospitals devoted exclusively to the treatment of cancer because such institutions must be situated in centers of large population. It is obvious for economic and social reasons that the practical needs of the average community are best met by the cancer clinic in a general hospital. Since only a relatively small number of patients suffering from cancer can be taken care of in institutes and hospitals devoted to the treatment of cancer, the general hospitals throughout the country have the serious responsibility of caring for the greater proportion of patients with cancer. The organization of such a clinic has been described in a previous article.[1]

In addition to facilities for roentgen diagnosis, it is essential that the tumor clinic in a general hospital be supplied with a high voltage x-ray machine of sufficient voltage to insure effective external irradiation. Such a therapeutic unit should have a peak strength of 200,000 volts, which is the standard for most therapeutic x-ray machines in the United States today. The machine may be air cooled or water cooled at from 20 to 30 milliamperes; the latter set-up is more economical and time saving, particularly when there are many patients to be treated.

THE DISTRIBUTION OF RADIUM

At the Memorial Hospital many requests have been received for information concerning the amount of radium necessary for effective radium therapy in a general hospital or in private practice and the proper distribution of this radium in various applicators. Many visitors

From the Memorial Hospital for Cancer and Allied Diseases, New York, and the Josephine Lendrim Tumor Clinic of the Paterson General Hospital, Paterson, N. J.

1. Pack, G. T.: The Organization of a Tumor Clinic in a General Hospital, Surg., Gynec. & Obst. **58**:248-254, 1934.

to this institution either are engaged to some extent in the treatment of cancer or contemplate the organization of a clinic for this purpose. They not only are interested in the routine diagnostic and therapeutic measures at the Memorial Hospital but seek to apply this information to their own needs. They see in daily use almost 4 Gm. of radium in solution in an emanation plant, another 4 Gm. in a radium element pack for external irradiation, a battery of high voltage x-ray machines, a General Electric x-ray unit operating at from 700,000 to 1,000,000 volts, a Heublein teleroentgenotherapeutic unit for diffuse irradiation to the entire body at from 10 to 12 feet (305 to 365 cm.), skin plaques, trays and vaginal bombs with values of from 1,000 to 2,000 millicuries and gold radon seeds in abundance for every need. The diagnostic pro-

Fig. 1.—Diagnostic and therapeutic unit of a tumor clinic.

cedures and the surgical principles employed at this institution are readily utilized elsewhere, but the technic of radiation therapy may not be at all practical or suitable for general hospitals or tumor clinics in smaller communities, where such equipment is seldom available. The interns graduating from the six months' service at the Memorial Hospital and even the clinical fellows on completion of their three year course experience great difficulty in their new locations with the limited quantities of radium usually available, the form of applicators in which the radium is disposed, the new technical methods of treating cancer with a small amount of radium and the cost of gold radon seeds when purchased elsewhere.

What is the minimal quantity of radium necessary for a tumor clinic? How should the radium be distributed among the various applicators? What is the approximate cost of the radium and the equipment for its use? These problems are very important at this time, when so many new cancer clinics are being organized throughout the United States. No arbiter dares to specify the absolutely minimal number of milligrams of radium essential for all hospitals. The purchaser must consider such data as the population of the city, the death rate from cancer in the city, the estimated number of cases of cancer in the community, the number of beds in the hospital housing the tumor clinic, the proportion of patients with cancer in the past experience of the hospital and the prospective rate of growth of the tumor clinic and its future needs. I am not championing small quantities of radium against a larger supply, as I believe that every tumor clinic should own as much radium as possible. If a gram of radium is owned, it may be best to place it in solution in an emanation plant (approximate cost $6,000) and employ radon rather than radium element. If greater quantities of radium are available (2 Gm. or more), a radium element pack in a permanent fixed applicator may be used for external irradiation (teleradium therapy) in lieu of or supplementary to high voltage roentgen rays. The radium element (i. e., radium salt) is the form generally found suitable for amounts of less than 500 mg.

The quantity of radium should be sufficient to care for all cancers, but there should not be any in excess of this amount, as idle radium is too expensive. The radium may be purchased in such a flexible arrangement that the entire amount can be used interchangeably in the breast, uterus, mouth or skin. The radium may be arranged in such a distribution that additional milligrams may be added to the supply from time to time without disturbing the general scheme, the technic or the type of radium applicators. I can best illustrate these points by citing the experience of the Josephine Lendrim Tumor Clinic of the Paterson General Hospital in Paterson, N. J. This general hospital, with a capacity of 325 beds, is located in a city of approximately 150,000 inhabitants. Five years ago, through the generosity of Mr. Hugh Lendrim, I was given carte blanche in organizing this tumor clinic and planning the distribution of radium and the equipment for its application. The plan was so successful that later I introduced it into the tumor clinics of the Yale School of Medicine and the College of Medicine of Ohio State University.

The radium salt is distributed in individual platinum cells, measuring 11.5 mm. in length, 1 mm. in external diameter and 0.2 mm. in wall thickness. These individual radium cells were first employed by Sluys of Belgium. I introduced them into the United States five years ago

and have constructed this plan of radium therapy around these units. The radium content of each cell is either 1.33 mg. (delivering 10 microcuries destroyed hourly) or 3.33 mg. (delivering 25 microcuries destroyed hourly). The quantity of radium might be 2 and 5 mg., a distribution that is more common in the United States, but the expression of dosage by the Continental notation of "millicuries destroyed" for interstitial irradiation is more quickly arrived at by using the former plan. The platinum cells of uniform size and shape are kept in a specially designed container, which affords filtration and protection. The number of these cells, containing a total quantity of 130 mg. of radium, and the various applicators in which they are used are summarized with specifications in one of the following tabulations.

The radiologist seldom has occasion to use more than 130 mg. of radium in the treatment of any one cancer, provided supplementary high voltage x-rays are available. These platinum cells containing radium may be used without additional filtration on superficial lesions of the skin or in wax moulages for irradiation of cancer of the lip, or all these cells (totaling 77) may be grouped together in any of the various skin plaques or trays. Furthermore, they may be placed in special applicators for irradiation of the vagina or in a bomb for radium therapy of the uterine cervix. The volume of these seventy-seven tiny cells is quite small. The individual cells may be transferred to platinum capsules for esophageal or intra-uterine use or for employment in Curie colpostats, the capsules giving the additional filtration that is necessary for these locations. If interstitial irradiation is contemplated, the cells may be placed in hollow sheath needles with removable trocar points. These needles are available in various lengths and will hold one, two or four cells placed end to end. If a carcinoma of the tongue is to be irradiated interstitially, the short needles are loaded with single cells. If the next patient is to receive interstitial radium therapy for a carcinoma of the breast, the cells are transferred to the longer sheath needles, which will hold four cells.

This flexible distribution enables the clinic to obtain the greatest use of a small quantity of radium. It is an economical plan as it avoids a large initial expenditure for radium and keeps the radium constantly in use. It is obviously cheaper to buy various radium applicators, unfilled sheath needles and other supplies in quantity than it is to purchase an inflexible distribution of radium permanently arranged in capsules and needles of different lengths. For example, many radiologists have radium in quantities of 25 and 50 mg. in separate capsules for intra-uterine treatment; these fixed applicators are not suitable for intra-oral irradiation. Radium is also supplied in the form

of fixed needles which may be grouped and screened for use in the uterus, but on the whole this arrangement is not as convenient as the one just described.

In the following pages I shall describe briefly the principles and practice of radium therapy in a tumor clinic in a general hospital, realizing at the same time that these statements summarily given are dogmatic and often controversial. The technic of therapy to be given later for cancers of various locations is not necessarily what I consider

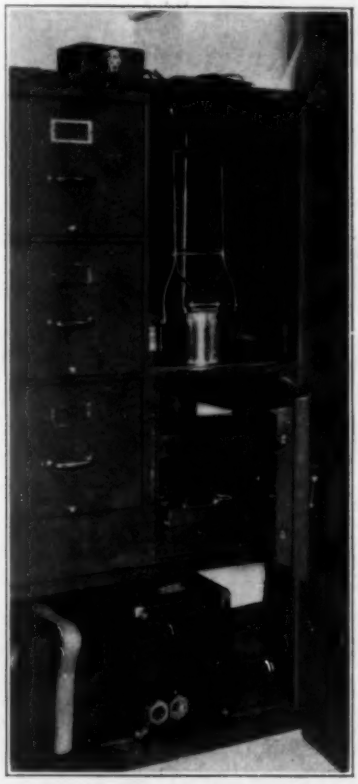

Fig. 2.—Closet enclosing built-in radium safe and cabinet for case histories.

to be ideal. For example, gold radon seeds are preferable in my opinion to radium needles for interstitial irradiation of cancers of the urinary bladder and oral cavity. The methods described in this article are based on the best utilization of a small quantity of radium element as used in tumor clinics in general hospitals. *The description is not a summary of the technic in use at the Memorial Hospital.*

The following tabulations present information concerning the equipment and distribution of radium for a cancer clinic.

Specifications for Radium (130 Mg.) and Containers for Tumor Clinic, with Estimate of Cost

All the radium is furnished in platinum cells 11.5 mm. in length, 1 mm. in external diameter and 0.2 mm. in wall thickness.

No. of Cells	Radium Content per Cell	Total No. of Mg.	Value
14	3.33 mg.	46.62	$1,631.70
63	1.33 mg.	83.79	2,932.65
		130.41	$4,564.35

14	Platinum cells. (The 14 cells containing 3.33 mg. are each gold-plated to distinguish them from the 63 cells containing 1.33 mg. each), at $4.00 each	$ 56.00
63	Platinum cells, at $3.25 each	204.75
6	Platinum-iridium tubes with bulldog eye, measuring 19.53 mm. in external length, 3.87 mm. in external diameter, and 0.3 mm. in wall thickness, each to contain 4 of the foregoing cells, at $20.00 each	120.00
1	Platinum-iridium tube with bulldog eye, measuring 19.5 mm. in external length, 4.13 mm. in external diameter and 12 mm. in internal length, to contain 8 cells	23.00
3	Special screw cap brass tubes of 1.5 mm. in wall thickness, 24 mm. in external length, 7 mm. in external diameter, 20 mm. in internal length and 4 mm. in internal diameter, at $2.50 each	7.50
10	Small platinum-iridium (20 per cent) needles with one eyelet and removable trocar point (Treves needles), measuring 17 mm. in length, 1.65 mm. in external diameter and 0.3 mm. in wall thickness. Each to hold 1 cell at $10.00 each	100.00
14	One cell gold sheath needles with removable platinum-iridium points, at $4.80 each	67.20
8	Two cell gold sheath needles with removable platinum-iridium points, at $5.40 each	43.20
12	Four cell gold sheath needles with removable platinum-iridium points, at $6.45 each	77.40
3	Brass plaques of varied sizes to hold the radium cells in the treatment of epithelioma of the skin, at $10.00	30.00
1	Tray or pack—distance applicator for radium. Designed to contain the platinum-filtered radium cells	18.00
10	Curie colpostats, at $0.85 each	8.50
1	Flat vaginal applicator or spoon (Healy model)	18.00
1	Bomb for surface irradiation of cervix (Bailey model)	25.00
1	Berven tonsil applicator for surface irradiation of tonsil	45.00
1	Intubation tube (O'Dwyer model) for larynx. Designed to hold radium cells within its circular walls	20.00
	Equipment for protection of radium workers	250.00
	Total	$5,677.90

It is suggested that a quantity of 250 mg. of radium, employing the removable platinum cell technic, be divided as follows:

1	Platinum-iridium tube containing a platinum cell permanently sealed in the tube, which has a bulldog eyelet. The over-all length of the tube is 21.7 mm.; the wall thickness, 0.5 mm. of platinum; the external diameter, 2.5 mm. This tube costs $20.00 and contains 26.64 mg. of radium (200 microcuries destroyed hourly)	26.64 mg.
4	Platinum-iridium tubes each containing a platinum cell permanently sealed in the tube. The over-all length of the tube is 21.7 mm.; the wall thickness, 0.5 mm. of platinum; external diameter, 1.9 mm. Each tube costs $12.75 and contains 13.32 mg. of radium (100 microcuries destroyed hourly)	53.28 mg.
51	Platinum cells, 11.5 mm. long with a wall thickness of 0.2 mm. of platinum, each to contain 3.33 mg. of radium	169.83 mg.
	Total	249.75 mg.

The tubes containing 26.64 and 13.32 mg. of radium are to be used for uterine irradiation, the 26.64 mg. tube being used for the cervix and one 13.32 mg. tube within the body of the uterus proper, the remaining three 13.32 mg. tubes in a Curie colpostat furnishing a proper combination for radium therapy of cancer of the cervix. A different arrangement is employed for carcinoma of the body of the uterus. The individual platinum cells are for the needles, tubes, plaques and moulages of various types.

Cost of Equipment for Protection of Radium Workers

Assembly table with lead shield $150.00

This table is devised to afford adequate protection to the worker who assembles the radium applicators. It is 32 inches (81.2 cm.) high, 48 inches (121.9 cm.) long and weighs 770 pounds (349.6 Kg.). It is readily portable owing to its mounting on four roller-bearing casters. A lead shield 13 inches (33 cm.) wide, 22 inches (55.8 cm.) high, 3⅛ inches (8 cm.) thick and weighing 550 pounds (249.7 Kg.) is erected at one end of the table. At the top of the shield is an adjustable lead glass plate to protect the eyes (design by Failla).

Assembly forceps with lead hand shield 20.00

The forceps for handling radium has a cup-shaped lead shield on its handle to protect the fingers from exposure to radiation.

Hand carrier for radium or radium applicators 40.00

A radium carrier, such as has been designed by Failla for use in the Memorial Hospital, is absolutely necessary to transport the radium and radium applicators. It is essentially a cylinder 7 inches (17 cm.) in diameter and 4 inches (10.2 cm.) deep, with a wall of lead of ½ inch (1.27 cm.) thickness, enclosed in a monel case. A handle 15 inches (38 cm.) in length supplements the protection afforded by the heavy filtration. The top closes automatically while it is carried.

Container for individual platinum cells of radium..... 40.00

When not in use the platinum cells containing the radium are kept in a lead box container made of hinged lead plates 1 inch (2.5 cm.) thick. Seventy-seven small countersunk holes are of sufficient size and depth to hold the platinum cells. In this arrangement the radium is constantly visible, the loss of a single cell is at once detected and the cells are easily grasped and removed when it is necessary to assemble the various applicators.

The specifications for the sheath needles are given in table 1.

TABLE 1.—*Specifications for Sheath Needles*

To Accommodate	Total Length, Mm.	Internal Length, Mm.	External Diameter, Mm.	Internal Diameter, Mm.	Wall Thickness, Mm.
1 cell (Treves needle).....	17.0	12.0	1.65	1.05	0.3 (platinum-iridium)
1 cell (gold sheath type).....	24.5	12.0	1.9	1.1	0.4 (gold)
2 cells (end to end).....	36.0	23.5	1.9	1.1	0.4 (gold)
3 cells (end to end).....	47.5	35.0	1.9	1.1	0.4 (gold)
4 cells (end to end).....	59.0	46.5	1.9	1.1	0.5 (gold)

The 0.4 mm. wall thickness of the gold sheath needles is equivalent to 0.3 mm. of platinum. The combined wall thickness of the gold sheath needle and the 0.2 mm. platinum cell is equivalent to 0.5 mm. of platinum.

The Treves radium needle [2] is a tiny single cell needle which is very serviceable in the interstitial irradiation of intra-oral cancers because of its small size. Platinum with 20 per cent iridium is used. The over-all length of the needle is 17 mm., the internal diameter 1.05 mm., the wall thickness 0.3 mm. and the external diameter 1.65 mm., which are the smallest dimensions of any interstitial radium applicator with the exception of the radon seed. The tip has a removable trocar point 2 mm. in length for the insertion of the cell into the needle. There is a space of 12 mm. in the bore of the needle to contain the platinum-radium cell. The total filtration of needle and cell is 0.5 mm. of platinum.

NOTATION OF DOSAGE

In America the dosage is expressed in terms of milligram hours or millicurie hours, which is a constant value, being the dose of emission of radium. It is computed by multiplying the intensity of the radiation (i. e., quantity: milligrams of radium element or millicuries of radium emanation) by the duration in hours of the application. The notation used throughout France makes the dose proportional to the quantity of radon destroyed during its application. This notation (Debierne and

2. Treves, N.: A Small Platinum Needle Designed for the Use of Various Strengths of Radium Element Interstitially, Am. J. Roentgenol. **33**:537-544, 1933.

Regaud, 1914; Regaud and Ferroux, 1919) is preferable because it is equally applicable to radium or radon and for expressing doses of external and interstitial radiation. Let it be assumed that the total therapeutic value of 1 millicurie of radium emanation is 133 millicurie hours. Therefore, 1 millicurie destroyed is the equivalent of 133 millicurie hours or of 133 milligram hours, or 1 milligram of radium acting for one hundred and thirty-three hours may be expressed in terms of dosage as 1 millicurie destroyed. One millicurie destroyed is equal to 1,000 microcuries destroyed. The radium element is distributed in platinum cells, each containing 3.33 or 1.33 mg. of radium, which give radiations equaling 25 and 10 microcuries destroyed hourly.

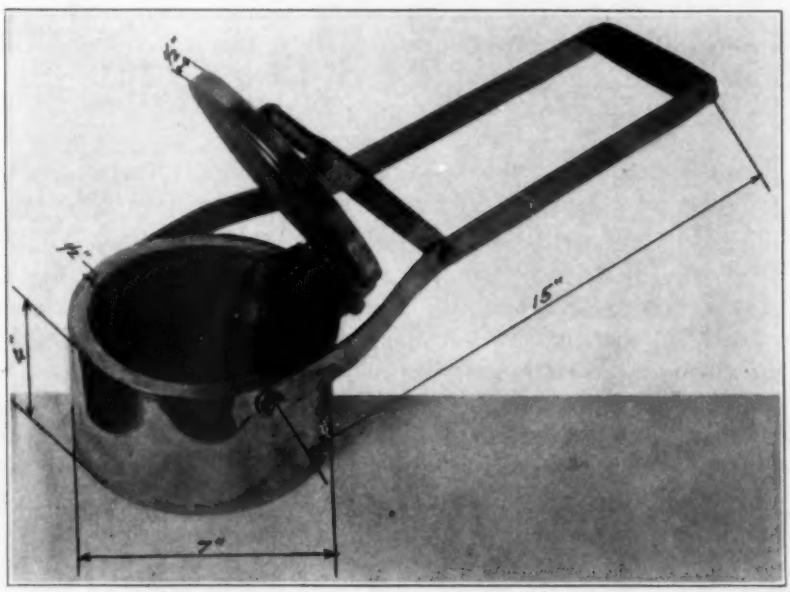

Fig. 3.—Radium carrier in a monel case, lead filled. The position of the handle determines the opening and closing of the lid. Protection is afforded not only by the heavy filtration of the walls but by the long handle (Failla model).

THE TIME-INTENSITY FACTOR

Some criticism has been leveled at this plan for radium therapy, because of the small quantity of radium available for any one treatment, i. e., the low intensity and long duration of such treatments. In fact, this is an advantage rather than a handicap, because the modern trend is to apply smaller quantities of radium for a longer time (within limits). At the Radium Institute of the University of Paris, where 9 gm. of radium is available, the use of capsules in the uterus and needles in the

tongue is favored. Both the capsules and the needles are of low radium content, and several days is required to deliver a cancerocidal dose. By such methods the radiotherapeutist may safely give a much larger total dose than would be possible with a greater intensity. My associates and I [3] have given abundant experimental proof to substantiate this theory in a previous article.

It seems logical to assume that a cancer cell or a tissue cell would not be indifferent to variations in the intensity of radiation. Such a cell, continuously engaged in self-repair, the ingestion, consumption and stor-

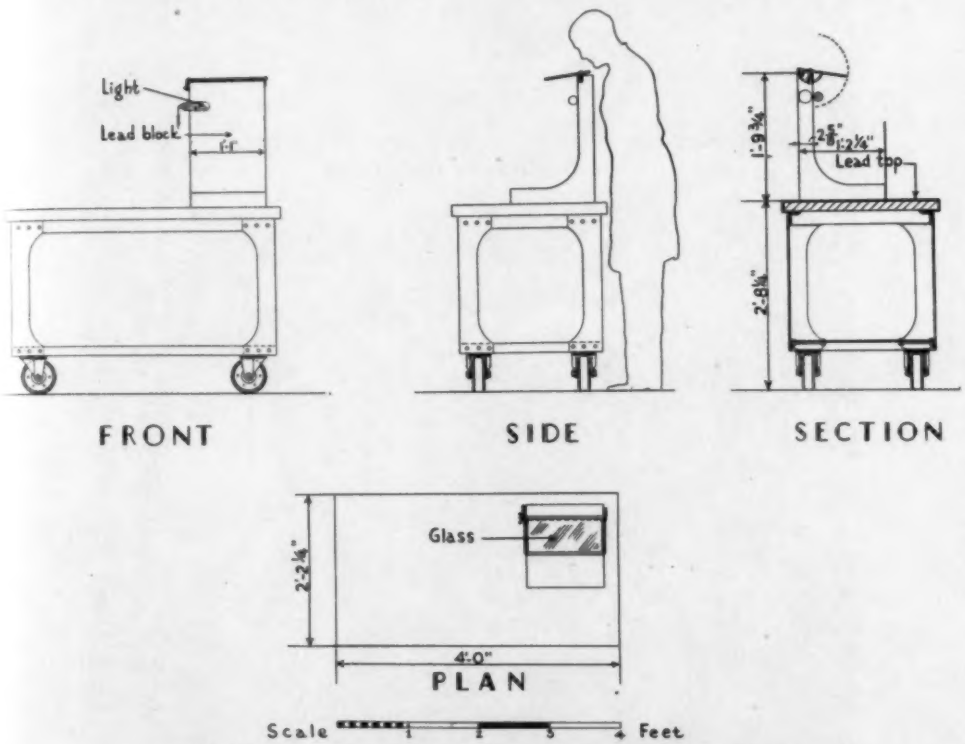

Fig. 4.—Diagram and plan of the radium assembly table.

age of food, the excretion of waste products, the pursuit of its specific function and possible preparation for cell division, and in delicate ionic balance with the tissue juices which bathe it, is a living unit and must be capable of making certain adjustments to the influences of noxious agents to which it is exposed, whether they are chemical or physical. All physiologic processes require time for their completion. If the doses were equal, the cell—either normal tissue cell or cancer cell—should be

3. Pack, G. T., and Quimby, E. H.: The Time-Intensity Factor in Irradiation, Am. J. Roentgenol. **28**:650-666, 1932.

more tolerant of prolonged irradiation of low intensity than of short irradiation of high intensity. The following two statements are generally accepted as biologic truths: (*a*) The susceptibility of any cell to irradiation varies considerably during the lifetime of the cell. (*b*) Different cells (e. g., cancer cells and normal tissue cells) vary greatly in radio-

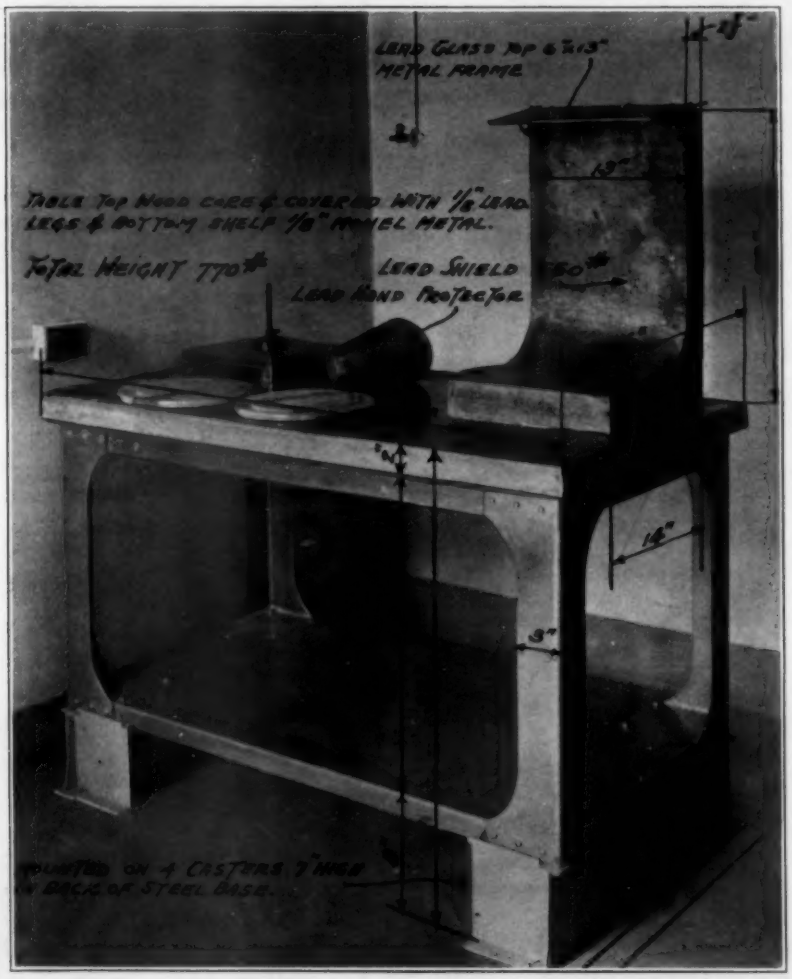

Fig. 5.—Radium assembly table. The mobile unit is designed to protect the technician while handling the radium and assembling the various applicators.

sensitivity. When these cells are irradiated, the radiosensitive and radioresistant cells as well respond with greater effects to higher intensity and shorter duration of irradiation, but it is conceivable that while the response is comparable in kind it is not necessarily so in degree. The end-result of successful irradiation is the destruction of the cancer cell

and the preservation of normal tissue cells; there is clinical and experimental evidence to suggest that long duration and low intensity of irradiation (within limits) have greater differential effects on tumor cells than on normal tissue cells.

Interstitial irradiation, even though more intense, may produce differential effects according to the intensity and duration of irradiation. Radon deposited interstitially has an exponential rate of decay, less than 1 per cent remaining at the end of thirty days. The irradiation by this interstitial method is therefore continuous but with diminishing intensity. There is some question concerning the relative effectiveness of continuous irradiation by radon with an exponential diminution in intensity or by radium element interstitially with a constant equal intensity and the same total dose. For all these reasons I am inclined to prefer a low intensity of constant radium value, even though this may require from

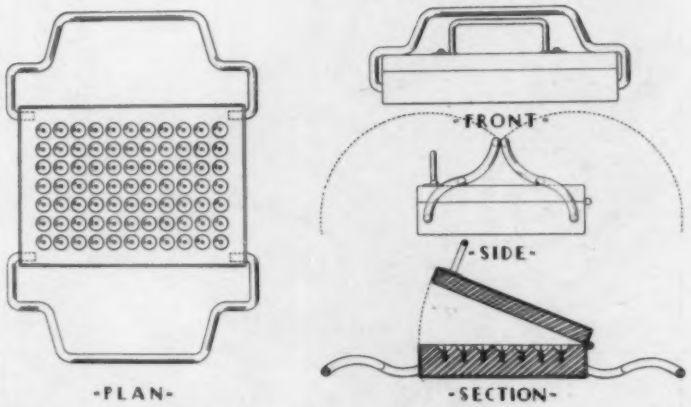

Fig. 6.—Permanent radium container for platinum cells. A monel box is lead filled to afford greater protection by filtration. Each platinum cell is in its individual counter-sunk hole, so that one may see at a glance whether or not all the cells are present. The arrangement requires less handling of the radium. A detachable long handle is provided to use for carrying.

five to ten days of continuous application (exclusive of preliminary external irradiation) in the case of cancer of the uterus and of the tongue.

RAPID CALCULATION OF RADIUM DOSAGE AND TIME OF EXPOSURE

Friedman of the New Haven Hospital, where this method is in daily use, has devised a slide rule which simplifies the calculation of exposure.[4]

4. Friedman, Irving: A Slide-Rule for Calculating Radiation Exposure When Cells of Uniform Radium Content Are Used, Radiology **2**:365-366, 1934.

On one side is a scale of logarithmic form, to compute the duration of exposure required in order to administer a desired amount of radiation with a given number of cells. On the other side is a scale of linear form, to determine the time of day when the exposure should be terminated.

The operation of this device can be explained by the following illustrative example (fig. 9): Suppose that a dose of 2,200 milligram

Fig. 7.—Radium container for platinum cells, in a monel case, lead filled.

hours (approximately 16.5 millicuries destroyed) is to be delivered to a cancer of the tongue and that eight needles, each containing 3.33 mg. of radium in a single cell, are required. The first sliding scale is adjusted so that the indicator points to 2,200 milligram hours of radiation. The required exposure is then read on the lowermost scale opposite 8, the number of cells, which in this case would be approximately eighty-three hours. The rule is then turned over, and the second sliding scale is

adjusted so that one of the two indicators points to 8 p. m., the hour the needles were inserted. From this it may be seen that the treatment is terminated at 7 a. m. of the fourth day, the day being read on the same side as the indicator which marks the beginning of the exposure. This rule is accurate to within a small fraction of 1 per cent.

CALCULATION OF DOSAGE

It is necessary to know and to plan the quantity of irradiation to be delivered to any tumor. As it is technically impossible to irradiate any tumor absolutely homogeneously, the radiotherapeutist adopts as the delivered or tissue dose the minimal quantity of radiation received at any point in the tumor; the rest of the tumor must therefore receive more than enough if the minimal dose delivered has the capacity of sterilizing the cancer. The tissue dose in the tumor is then of more importance than the applicator dose or dose of emission, because the latter notations do not indicate the quantity of radiation actually delivered into the tumor. These are best expressed in terms of biologic

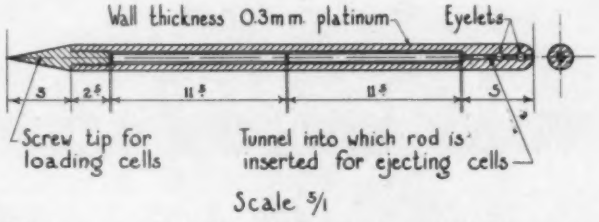

Fig. 8.—Diagram of a sheath needle designed to hold two removable radium cells.

units; such a unit is the threshold erythema dose used at the Memorial Hospital and is defined as that dose which in 80 per cent of the cases produces a faint reddening or bronzing of the skin in from ten to twenty days and in the other 20 per cent produces no visible effect. This threshold skin erythema dose may be the biologic unit for all tissue doses, whether delivered by external or by interstitial irradiation.

All radiation applicators, external, interstitial and intracavitary, are calibrated by this common biologic unit, so that the tissue dose can be estimated at all depths below the surface of the skin and in tumors of all dimensions. This technic has been the work of Quimby and is outlined in summary here. The applicator dose necessary to produce the threshold erythema dose is found by direct experimentation; then the percentage of the amount falling on the skin, which reaches various depths, is determined by means of a water phantom and small ionization chamber. The tissue dose delivered in the tumor by external irradiation is considered as the dose delivered at that point which lies deepest or at

the greatest distance from the skin portal.[5] The tissue dose can be calculated properly only when the primary tumor and its metastases are measured in all diameters; the exact depth from skin portals must also be recorded. The calculation of tissue dosage for interstitial irradiation is based on the practice of considering all tumor masses as lying just within a sphere or composed of two or more adjacent or overlapping spheres, each of which is treated individually in the case of long narrow tumors (Martin and Quimby). Quimby has devised a table giving the quantities of radiation from interstitial sources necessary to deliver specified minimum threshold erythema doses in various spherical volumes (table 2). This table is invaluable to the clinical radiotherapeutist, as it

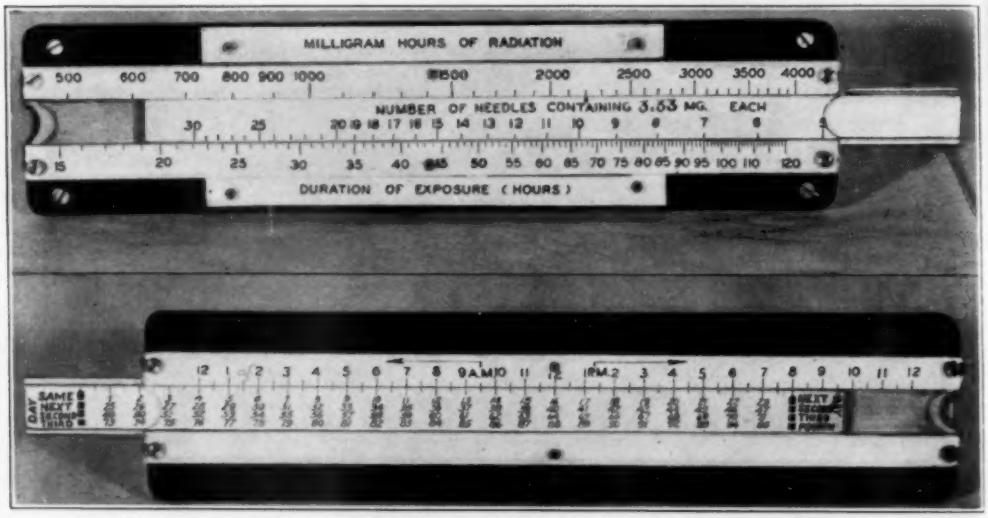

Fig. 9.—A slide rule for the rapid calculation of dosage of radium and time of exposure. The logarithmic and linear forms are based on the platinum cell as a unit, each to contain 3.33 mg. of radium.

enables him at a glance to know the exact quantity of interstitial radiation necessary to deliver any desired tissue dose in a tumor of any size.[6]

Clinical experiments with cancers of the mouth, breast, bladder, skin, rectum, stomach and prostate have demonstrated that the lethal tissue dose for malignant tumors of these organs varies from 3 to 10 threshold erythema doses, depending on the radiosensitivity and on other factors. A specific example of the applicability of this method may be worth

5. Martin, H. E.; Quimby, E. H., and Pack, G. T.: Calculations of Tissue Dosage in Radiation Therapy, Am. J. Roentgenol. **25**:490-506, 1931.

6. Quimby, E. H.: Physical Factors in Interstitial Radium Therapy, Am. J. Roentgenol. **33**:306-316, 1935.

while here.[7] A mammary carcinoma with a volume of 60 cc. has already received a total of 3 threshold erythema doses from fractionated high voltage x-rays cross-firing through two ports. A total tissue dose of 7 threshold erythema doses is required, so that the rest (7 — 3 threshold erythema doses), or 4 threshold erythema doses, must be given by interstitial methods. According to table 2, this would be 4,550 milligram hours, or 34 millicuries destroyed. This dose is then administered by the insertion of radium element needles. The dosage table is strictly applicable only for radium needles to be left in place four days or longer; when the time of irradiation is less, allowance is made by decreasing the quantity of radiation used.[8]

Quimby employed radium needles of various lengths (0.5 mm. platinum filter) in detailed experiments on rabbit muscle and butter

TABLE 2.—*Quantities of Radiation from Interstitial Sources Necessary to Deliver Specified Minimum Doses in Various Volumes* *

Threshold Erythema Doses	Volume, Cc.										
	10	20	30	40	60	80	100	125	150	200	250
	Millicurie, or Milligram Hours										
1	275	380	470	530	650	750	845	955	1,060	1,250	1,410
2	550	760	940	1,060	1,300	1,500	1,690	1,910	2,120	2,500	2,830
3	825	1,140	1,410	1,590	1,950	2,250	2,535	2,865	3,180	3,750	4,240
4	1,100	1,520	1,880	2,120	2,600	3,000	3,380	3,820	4,240	5,000	5,660
5	1,375	1,900	2,350	2,650	3,250	3,750	4,225	4,775	5,300	6,250	7,070
7	1,925	2,660	3,490	3,710	4,550	5,250	5,915	6,685	7,420	8,750	9,900
10	2,750	3,800	4,700	5,300	6.500	7,500	8,450	9,550	10,600	12,500	14,100
	Millicuries Destroyed										
1	2.1	2.9	3.5	4.0	4.9	5.6	6.4	7.2	8.0	9.4	10.6
2	4.2	5.8	7.0	8.0	9.8	11	13	14	16	19	21
3	6.3	8.7	10.5	12	15	17	19	22	24	28	32
4	8.4	12	14	16	20	22	26	29	32	38	42
5	10.5	14	18	20	24	28	32	36	40	47	53
7	15	20	24	28	34	39	45	50	56	66	74
10	21	29	35	40	49	56	64	72	80	94	106

* These doses are for needles to be left in place four days or longer. If they are to be removed in two or three days, all quantities of radiation should be about 10 per cent less. A platinum filter of from 0.3 to 0.5 mm. was used.

decoloration and from these studies formulated certain rules which are important whenever linear radium foci are to be used interstitially. Distances of from 1.5 to 2 cm. are recommended as the proper spacing of the needles in a single parallel series.[9] For two series in parallel planes, she advised that the needles should never be placed farther apart than the distance between the planes, and even closer spacing may be

7. Lee, B. J., and Pack, G. T.: Tissue Dosage Estimation in Mammary Cancer, Bull. Memorial Hosp., New York **1**:67-73, 1929.

8. Quimby, E. H.: Determination of Dosage for Long Radium or Radon Needles, Am. J. Roentgenol. **31**:74-91, 1934.

9. Quimby, E. H., and Stewart, F. W.: Comparison of Various Sources of Interstitial Radiation, Radiology **17**:449-470, 1931. Quimby, E. H.: A Comparison of Radium and Radon Needles and Permanent Radon Implants, Am. J. Roentgenol. **23**:49-56, 1930.

advantageous. The needles are of such length that the active radium-bearing portions extend completely beyond the limits of the tumor. In practice, the volume of tumor irradiated is considerably larger than the actual measurements of the tumor. The periphery of the lesion should receive a heavily concentrated dose, as it is most needed at the growing edge of the tumor. If the radium needles are placed more widely apart, the dose per needle or per centimeter of needle length must be much greater than when they are close together. Such intense doses may lead to radionecrosis around each needle. The length of the implant has also been given consideration by Quimby. For a given number of millicurie or milligram hours, the longer the radium needle the shorter the distance at which a given dose is delivered by the needle, or conversely, the greater the amount of radiation necessary to deliver 1 threshold erythema dose at a given distance. The quantities of radiation necessary to deliver 1 threshold erythema dose at a distance of 1 cm. for radium needles of various lengths, each with a 0.5 mm. platinum filter, are given in Quimby's table (table 3). These facts are fundamentally essential in the employment of the radium needles described in this text.

TABLE 3.—*Quantities of Radiation Necessary to Deliver 1 Threshold Erythema Dose at 1 Cm. from Needles of Various Lengths* *

Length of Needle, Cm.	Quantity of Radiation	
	Millicuries or Milligram Hours	Millicuries Destroyed
0.5	115	0.85
1.0	130	1.00
1.5	144	1.1
2.0	158	1.2
3.0	186	1.4
4.0	220	1.6
6.0	285	2.1
8.0	370	2.8
10.0	475	3.6

* A platinum filter of 0.5 mm. was used.

RENTAL OF RADIUM FOR MAINTENANCE OF CLINIC

It is not the purpose of this article to present any plan for financing a tumor clinic. The Josephine Lendrim Clinic of the Paterson General Hospital as well as certain other tumor clinics in general hospitals are sufficiently endowed to care for all indigent patients who apply but cannot pay for treatments. The complete facilities of the clinic are tendered to all patients with cancer, regardless of their financial status. For those who can pay, a small registration fee is collected at the first visit, and a small charge is made for subsequent dressings, when this is necessary. Because of the many inquiries received concerning the rental rates of radium, I am presenting herewith a scale of prices used in the Josephine Lendrim Clinic, realizing at the same time that these

charges, while flexible, may not be suitable for clinics in other communities. The patients applying to the tumor clinic are classified by the social secretary into four groups, based on an appraisal of their financial status. These are as follows: *A*, private patients; *B*, semiprivate patients; *C*, clinic patients and *D*, special patients who cannot afford the regular rates. The charges are made for each 1,000 milligram hours consumed and are subdivided according to the following plan:

Grade of Patient	A	B	C	D
Rate per 1,000 milligram hours	$20.00	$10.00	$ 5.00	$3.00
Minimal charge	40.00	20.00	10.00	5.00

On this basis, a semiprivate patient who receives 3,000 milligram hours of radium will pay the hospital $30. A clinic patient who receives 1,500 milligram hours of radium therapy will pay the hospital the minimal charge of $10. The money so obtained is used solely for the maintenance of the clinic.

TREATMENT OF CANCER

Epithelioma of the Skin.—This superficial and accessible cancer may be treated successfully by any one of a number of methods of radiation. A careful observance of the response of this type of tumor to radium and roentgen therapy affords a good object lesson in the technical details and physical principles involved. In the majority of cases cancer of the skin may be cured by low voltage roentgen therapy, very light filtration or no filtration being employed. Unlike cancer of other regions, epithelioma of the skin is usually treated by a single application of radium or x-rays. The same methods, principles and dosage are applicable to squamous cell carcinoma and to basal cell carcinoma of the skin, provided the size and degree of infiltration are equal. The basal cell epithelioma is a relatively radiosensitive lesion, except when bone or cartilage is invaded; the development of adenoid features indicates a greater radioresistance.

In lieu of the individual moulages which are used for radium treatment in particular cases, the tumor clinic may find a series of plaques suitable for the majority of epitheliomas of the skin. These plaques have different dimensions for their radiating surfaces, but all have the same filter and are applied at a distance of 1 cm. They are modifications of the applicators designed at the Memorial Hospital by Dr. Failla. A small plaque, 1.8 cm. square, has a radiation surface of 2 sq. cm. The floor, or filter, of the plaque is a 2 mm. plate of brass, to which should be added the 0.2 mm. of platinum for the radium-bearing cells which fit into the brass plaque. A similar plaque, rectangular and measuring 2.7 by 1.7 cm. in diameter, has a radiating surface of 3.75 sq. cm. A larger

round plaque with a diameter of 4 cm. and a radiating surface of 7 sq. cm. is also useful in the treatment of lesions of greater dimensions. The interiors of these boxlike plaques are subdivided into loges devised to hold the radium cells. The radium-skin distance is constantly 1 cm., and this distance is obtained by the intervention of blocks of balsa wood 1 cm. in thickness. The dose varies from 700 milligram hours in the case of the small, square plaque to as high as 2,000 milligram hours for the larger, round plaque (fig. 10).

The radium tray is a small external applicator for radium therapy; the radium is applied in it at a distance of 3 cm. from the skin. The

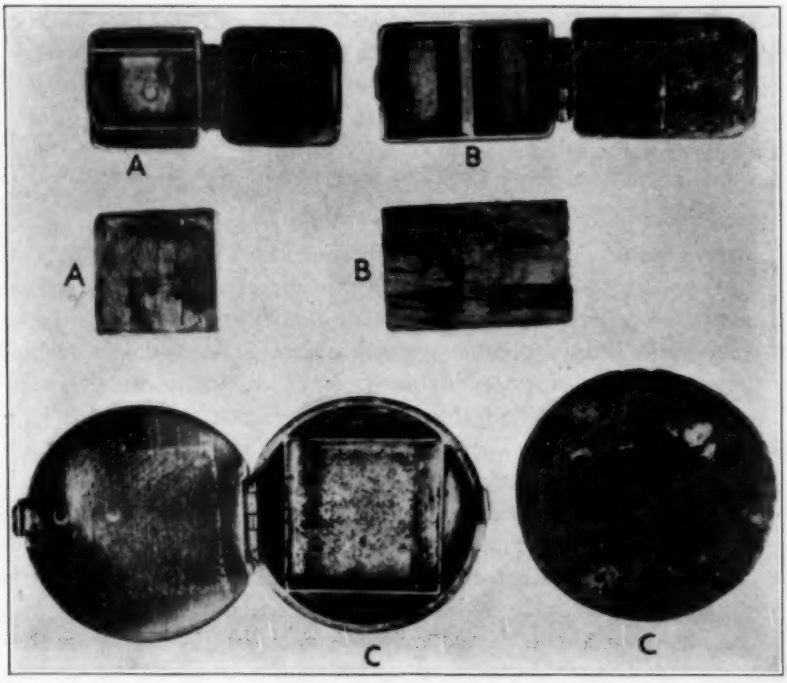

Fig. 10.—Plaque containers for superficial radium therapy of cancer of the skin. The compartments are of the proper size to contain the platinum cells of radium. All of the cells may be placed in any one of these plaques. The three models (*A*, square plaque; *B*, long or rectangular plaque, and *C*, round plaque) are shown with their respective blocks of balsa wood (1 cm. thick) used to give the proper radium-skin distance.

filter is also 2 mm. of brass, which is supplemented by the filtration strength of the radium cell, i. e., 0.2 mm. of platinum. The distance is obtained by a circular box or short cylinder, on the top of which is an especially designed tray or radium container. The interior of this tray is grooved by a serrated comb, by means of which the radium cells are distributed properly over the surface. On top of this is placed an addi-

tional small compartment for odd radium tubes. The radium tray gives a greater depth dose than the small radium plaques and is therefore useful in the treatment of the carcinoma of considerable depth, such as the recurrent mammary carcinoma in the skin or tumors of the parotid glands (fig. 11).

If the tumor projects to any considerable height above the surface of the skin, the quantity of radiation necessary to sterilize the base of the tumor can be materially lessened by removal of the superficial portion by endothermy. The focal distance of the radium from the skin depends on the size and the type of the lesion to be treated. The deeply

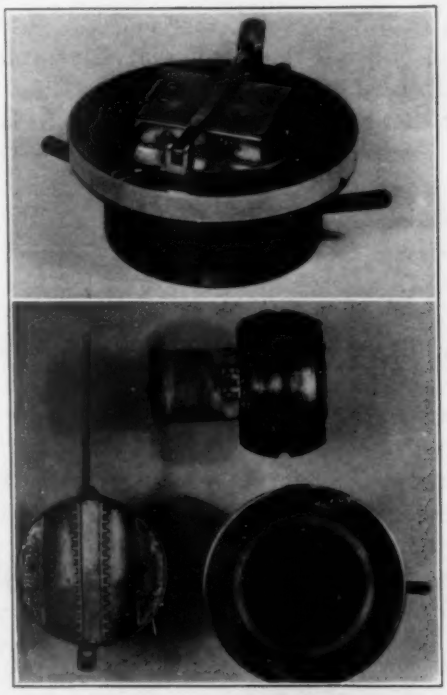

Fig. 11.—Radium tray for use at 3 cm. distance from the skin. The instrument is photographed assembled and dissembled to show the arrangement for the platinum radium cells. The accessory small brass box on the cover is for supplementary radium.

infiltrating carcinoma and the carcinoma with a large surface dimension require an application of radium at greater distances than is necessary for the small superficial epithelioma. This distance is obtained in many cases, particularly for the epithelioma of irregular outline and on uneven skin surface, by the intervention of a wax which is transparent to the gamma rays of radium. The formula for this wax is 100 Gm. of yellow wax, 100 Gm. of paraffin fusible at 62 C. and 20 Gm. of finely

sifted sawdust. This mixture is melted into sheets 1 cm. thick. It softens readily at 48 C. and is molded over the tumor until it hardens into a permanent moulage. The mixture can be sterilized at 120 C. and used again. It is said that this wax has approximately the same absorption coefficient as the skin. It is also maintained that, unlike dental modeling compound, it does not give off many secondary beta rays during the permeation by the gamma rays. If the cancer of the skin is small and flat, the focal distance may be only 0.6 cm., but if it is elevated or a large lesion, the distance is correspondingly greater, as from 1 to 1.5 cm.[10]

In general, the dose per unit of surface is increased with the thickness of the intervening wax (radium-skin distance), augmented with the thickness of the filter and diminished with the extent of the surface irradiated, without mentioning the influence exercised on the estimation of the dosage by biologic factors, such as differences in radiosensitivity. Regardless of the histologic grading of the carcinoma, the dose selected is usually the one capable of sterilizing the most radioresistant epidermoid carcinoma, with preservation of the normal tissues. This dose varies from 0.8 to 5 millicuries destroyed (from 100 to 650 milligram hours) per square centimeter of surface irradiated; e. g., for a small epidermoid carcinoma, such as one 2 sq. cm. in area, the dose may be 4.5 millicuries destroyed per square centimeter of tumor, but for a larger carcinoma, such as one 25 sq. cm. in area, the dose may be only 2 millicuries destroyed (266 milligram hours) per square centimeter of tumor.[11]

Occasionally the radiotherapeutist must employ interstitial irradiation for the larger, deeply infiltrating epithelioma of the skin. The small single cell needles are inserted in a radial or grid distribution through and beneath the tumor, the points of insertion being immediately peripheral to the margin of the tumor. The needles may thus be anchored to normal skin and are not easily dislodged. The dose depends on the estimated cubic content of the epithelioma and may be derived from table 4.

Malignant Melanoma.—The treatment for the malignant melanoma is wide, radical surgical excision, preferably with the endotherm knife. The tumor should be handled with extreme gentleness during its removal. Frank E. Adair and I have studied over four hundred cases of this type of tumor at the Memorial Hospital and found only seven-

10. Pack, G. T.: Radium Therapy of Tumors of the Skin at the Curie Institute of the University of Paris, Arch. Dermat. & Syph. **18**:286-289 (Aug.) 1928.

11. Pack, G. T.: Radiation Therapy of Cancers of the Orbitopalpebral Region at the Radium Institute of the University of Paris, Arch. Ophth. **57**:246-253 (May) 1928.

teen in which the growth exhibited any appreciable response to irradiation. Radiation therapy alone is not sufficient to control the growth and metastasis of this tumor, nor is it of prophylactic value in the treatment of the regional lymph node areas. In the treatment of melanoma of the extremities I am committed to prophylactic inguinal or axillary dissection, reserving radiation therapy for postoperative use in order to induce firm scarring and possible imprisonment of residual melanoma cells (abortive fibrosis).

Neurogenic Sarcoma.—In the majority of cases of neurosarcomas the neoplasm is radioresistant. The several factors which militate against successful radiation therapy are: first, the inherent radioresistance of the disease, even the very cellular neurosarcoma; second, the location of the tumor in regions which will not tolerate intensive irradiation well; third, the poor vascular supply to the tumor, which with its density accounts for frequent ulceration and radionecrosis after treatment, and fourth, the multicentric origin of the tumor. Cure has been obtained in a few cases by interstitial irradiation, needles containing

TABLE 4.—*Radium Applicators for Epitheliomas of Skin* *

Type	Size	Area Radiating Surface, Sq. Cm.	Radium Skin Distance, Cm.	Dose in Milligram Hours
Square plaque	1.8 cm. square	2.0	1	700-800
Long plaque	2.7 cm. by 1.7 cm.	3.75	1	1,000-1,200
Round plaque	4 cm. in diameter	7.0	1	1,400-1,600
Tray	6.2 cm. in diameter	17.5	3	3,000-3,500

* The filter used for all types was 2 mm. of brass and 0.2 mm. of platinum.

one, two or four platinum cells being used in tandem. In other cases a neurosarcoma has regressed with external irradiation alone; this response is not rapid, as in most malignant tumors, but is a slow, progressive diminution in size, due apparently to the conversion of the tumor into a fibrotic mass. The treatment of choice continues to be wide surgical excision and avulsion of the involved nerve, if identified, followed by heavy external irradiation. In some cases, particularly those of recurrent tumor, amputation is necessary.

Cancer of the Lip.—Cancer of the lip is irradiated from three sides by the surface application of a wax moulage in which the radium cells are implanted. The wax is either the wax described earlier in this paper or dental modeling compound. The size and shape of the epithelioma are cast in the moulage (fig. 12). The small radium cells are then embedded in the inner surface of the moulage corresponding to the site of the epithelioma and a surrounding area from 1 to 1.5 cm. The focal distance thus obtained is approximately 0.5 cm. and is determined by the thickness of the intervening wax. The filter used is

only 0.2 mm. of platinum. Each platinum-filtered radium cell used to deliver the dose contains 3.33 mg. of radium, which gives off 25 microcuries destroyed hourly. The average dose is from 0.75 to 1 millicurie destroyed (133 milligram hours) for every square centimeter of tissue treated. This dose varies according to the surface dimensions and the depth of infiltration of the carcinoma. The time of application is from eighteen to thirty-six hours. If the carcinoma infiltrates the lip deeply, it may be necessary to resort to interstitial irradiation, in which case the Treves platinum-filtered needles, each containing one radium cell, are inserted in parallel arrangement through the vermilion border of the lip deep into the substance of the tumor. Although radium has largely supplanted surgical intervention in the treatment of labial epi-

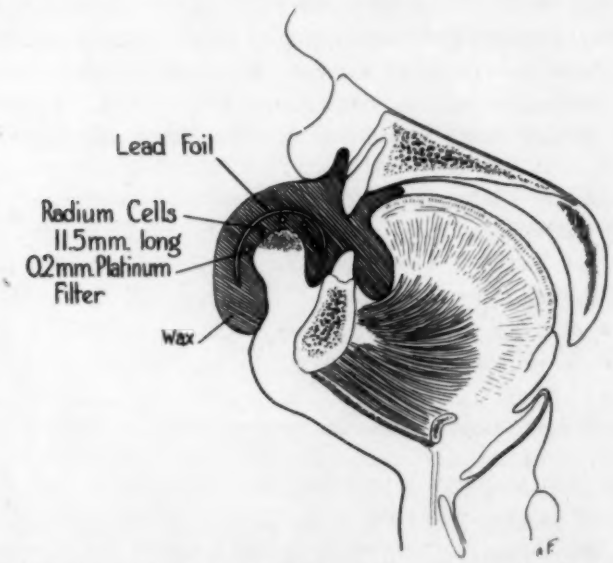

Fig. 12.—Moulage of wax or dental modeling compound used in the radium treatment of carcinoma of the lip.

thelioma, extensive surgical excision of the lower lip with plastic closure must be resorted to for (*a*) bulky, fungating infected carcinoma, (*b*) local recurrence after incomplete surgical excision and (*c*) local recurrence after inadequate irradiation. The methods of cheiloplasty employed are modifications of the operations of Bernard and Estlander devised by Hayes Martin.

Cancer of the Tongue.—The comparative malignancy and radiosensitivity of lingual cancer in various locations ascend in the following order: dorsolingual anterior cancer < infralingual cancer < dorsolingual posterior cancer. The papillary cancer is less malignant than the ulcerative, infiltrative cancer in the same location. In most instances

the epidermoid carcinoma of the mouth is not more radioresistant than the epidermis from which it is derived and generally it is less radioresistant. The dosage for sterilization of cancer of the lip, mouth or pharynx is from 75 to 100 per cent of the epidermicidal dose.[12] As computed experimentally with the use of gold radon seeds, this dose is approximately 8 threshold erythema doses.[5] This figure cannot be applied exactly to the dose delivered by radium needles, as the radiation here is linear in distribution rather than a point source, as in the case of the gold radon seed. For practical purposes, however, the dose delivered by radium needles is only slightly less than that employed with gold radon seeds.

In the treatment of cancer of the tongue the teeth are thoroughly cleansed, pyorrhea is treated and the necessary dental extractions are performed before radiation therapy is started. The mouth is cleansed by daily irrigations with saline solution or a solution of potassium permanganate during the course of treatment. While radioactive foci are within the mouth, the radium-bearing tissue is surrounded by a lead-filtered wax moulage held in place by the teeth and protecting the remainder of the mouth from the injurious and unpleasant effects of diffuse radiation.

The hollow needles employed for interstitial radium therapy of cancer of the tongue and of the floor of the mouth are of three sizes. Small platinum-iridium needles have been designed by Norman E. Treves which are admirably suited for the treatment of a small cancer in the floor of the mouth or in the lip, cheek, tonsil or palate; each needle holds one platinum cell of radium and has one eyelet and a removable trocar point. It is only 17 mm. in length and has a wall thickness of 0.3 mm., which, with the inner platinum cell, affords a total filtration of 0.5 mm. of platinum. Other hollow needles are of gold sheath design and contain one or two platinum-filtered radium cells (end to end). They are of similar design but somewhat longer, measuring 24.5 and 36 mm., respectively, with internal lengths (true linear focus of radium) of 12 and 23.5 mm. The total filtration when ready for use is the equivalent of 0.5 mm. of platinum. These needles are more suitable for use in the tongue. The true focus, i. e., the length of the needle occupied by the radium, is such that it will give a cylinder of irradiated tissue rather than a sphere, as obtains with the use of radon seeds (fig. 13).

Regional anesthesia is used, and the needles are introduced into the tongue and completely buried there. Each gold sheath needle has a

12. Regaud, C.: On Curietherapy of the Epitheliomata of the Tongue and of Their Following Adenopathy, Brit. J. Radiol. (B. A. R. P. Sect.) **30**:361-367, 1925.

double eye; the lower eye is for suturing the needle with silk thread to the neighboring lingual tissue; the upper eye is for external anchorage by means of a heavy thread which passes out of the mouth. It is important that the buried needles are parallel with each other. Furthermore, the needles must be a distance of 1 cm. or more apart from each other in order to prevent possible necrosis from too intense radiation and from secondary rays flying from adjacent needles.

Ordinarily about one-half as many platinum cells of radium are employed in the interstitial treatment of oral cancer as there are millicuries destroyed in the total dose; e. g., if the total dose is to be 20

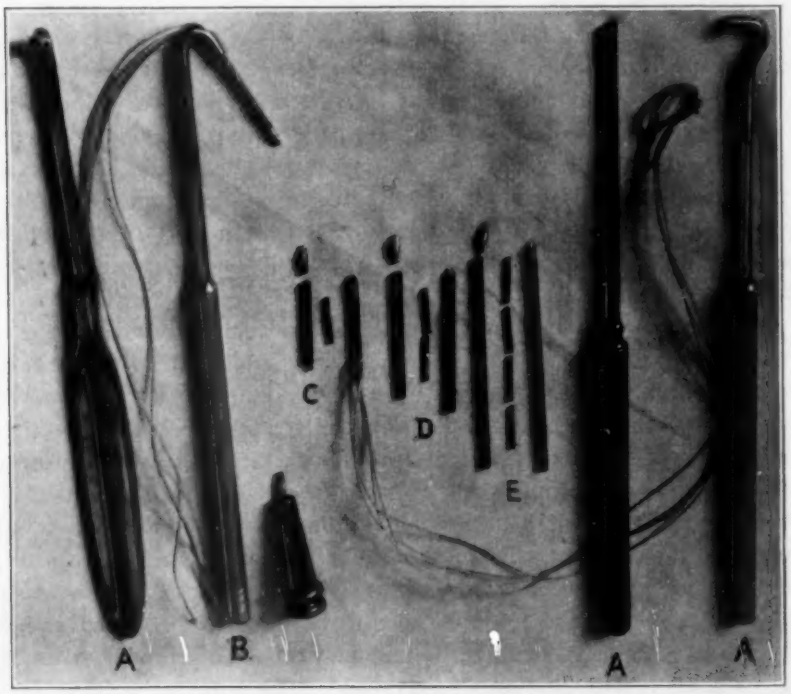

Fig. 13.—*A* are types of angled insertors for radium needles. *B* is an insertor with threaded radium needle attached; *C*, assembled and dissembled sheath needle designed to contain one platinum filtered radium cell; *D*, a sheath needle for two radium cells to be used in tandem formation, and *E*, a sheath needle for four radium cells.

millicuries destroyed, ten needles holding one cell of radium each are used. Occasionally long needles containing two cells of radium (end to end) are employed in the tongue, in which case correspondingly fewer needles are needed. These needles must sometimes remain in situ for as long as five days in order to deliver the required dose. The optimal dose per unit volume of tumor has been estimated approxi-

mately at 130 millicurie hours per cubic centimeter of tissue. This amount of radiation is sufficient to cause a marked reaction in the tumor and its environment but not enough to induce radionecrosis (fig. 14).

Radium therapy is of palliative benefit for cancer of the mouth in an advanced stage, but in such cases one cannot safely use the same rules as when a less advanced state of the disease permits an attempt at cure. In the intentionally palliative treatments, large doses are avoided and moderate successive irradiations are preferred to a single intense one.

The principles established by Regaud for the treatment of intraoral cancer are closely followed. These are summarized briefly as follows: (1) the distribution of numerous and weak radioactive foci in the cancer and surrounding tissue, care being taken to create a radiation field as homogeneous as possible; (2) the use of the gamma rays only in order to avoid a necrotizing effect; (3) continuous irradiation of low intensity for a long time, and (4) the use of a single treatment for successful results, as a carcinoma acquires radioresistance from prolonged and improperly spaced repeated irradiations.[12]

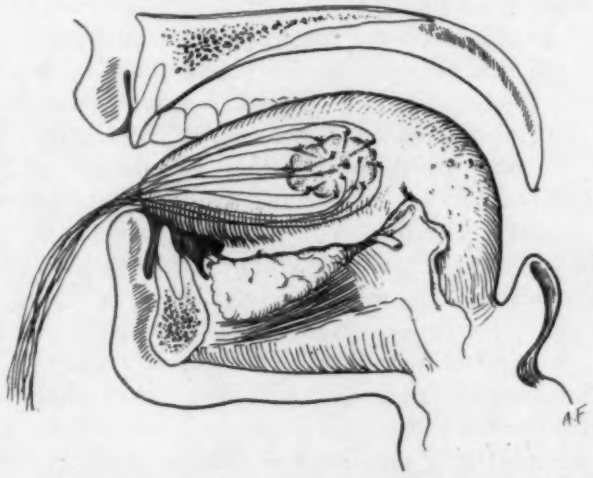

Fig. 14.—Method of interstitial radium therapy of lingual cancer. Each needle has two threads in double eyelets, one for suture and anchorage to adjacent normal tongue and the other to extend out of the mouth for fixation to the cheek.

Cancer of the lateral, anterior or dorsal surfaces of the tongue is readily treated by the previously mentioned procedures because of its accessibility. Interstitial radium therapy is superior to the surgical extirpation of such a cancer. A cancer situated on the posterior aspect of the tongue is difficult to treat because of its position; this same handicap obtains for surgical intervention even when the cancer in this location is small. Some of these lesions descend deeply into the

pharynx and hypopharynx and are poorly treated by radium puncture alone. Supplementary external irradiation is always given over the superior part of the neck prior to interstitial irradiation of the cancer in this location. Angled needle insertors are helpful in the treatment of cancer of the posterior part of the tongue. Cancer in this location and involving the valleculae may require supplementary interstitial irradiation; the radium needles may be inserted into the base of the tongue through the floor of the mouth anteriorly or through the submental or suprahyoid region, under the guidance of a directing finger at the base of the tongue.[13]

Cancer of the infralingual region and of the floor of the mouth, even when tiny, is seldom cured by surgical removal. If the cancer infiltrates deeply into the muscles of the tongue, interstitial irradiation of the infiltrating tumor must be carried out; however, there are certain dangers attendant on the interstitial irradiation of cancer in this location. Radium therapy of the floor of the mouth frequently causes radionecrosis; another dangerous complication is the occasional development of a phlegmon in the submental region. Superficial papillary carcinoma of the floor of the mouth may be treated satisfactorily by topical surface irradiation. For suitable cases an apparatus in the nature of a wax moulage is molded directly and applied to the floor of the mouth, bringing the radium cells in close approximation to the tumor and its environment. The tongue is protected by a lead shield during this treatment. Interstitial irradiation is occasionally contraindicated, if the cancer involves the mucous membrane covering the inferior maxilla. Carcinoma of the superior or the inferior alveolus is treated by the application of radium on a mold; if this is unsuccessful, the maxilla is resected and the site later irradiated by external radium therapy. After the direct irradiation of the floor of the mouth has been completed, or even prior to this in certain cases in which there is infection, the submental region is irradiated by means of high voltage x-rays, cross-fired through both submaxillary regions to concentrate on the floor of the mouth. The submaxillary and submental lymph nodes thus receive prophylactic irradiation, although this is of questionable curative value. If the lymph nodes are already palpable, the external irradiation is either preceded by neck dissection or followed by interstitial irradiation.

Malignant Tumor of the Tonsil.—A tonsillar neoplasm in most instances is radiosensitive and is managed well by external irradiation alone. The tonsil, tonsillar pillars, soft palate, pyriform sinuses and base of the tongue constitute Waldeyer's ring, a common site for such

13. Pack, G. T.: The Management of Intra-Oral Cancers at the Radium Institute of the University of Paris, Ann. Surg. **90**:15-25, 1929.

extremely radiosensitive tumors, such as the lympho-epithelioma and the transitional cell carcinoma. Even an epidermoid carcinoma in this location is usually anaplastic and labile to the effects of radium and x-rays. Tonsillectomy is always contraindicated.

The factors used in the sterilization of a tonsillar tumor by means of x-rays are: 200 kilovolts, 30 milliamperes, a target-skin distance of 60 cm. and a filter of 0.5 mm. copper and 2.5 mm. aluminum. Two lateral portals are used, the beams being directed through metal cones containing diaphragms and cross-fired through each posterior portion of the cheek and the upper part of the neck. A total dose of from 3,200 to 4,000 roentgens is given to each side by the fractionated method, with only 300 roentgens daily, alternating to each side of the neck. Three weeks is needed in which to deliver this dose.

Interstitial irradiation is seldom employed for tonsillar carcinoma unless the lesion does not show the usual response to well planned roentgen therapy; it must be employed cautiously because of the danger of late radionecrosis and hemorrhage from overdosage. The combination of external and interstitial irradiation is more practical and safer when the dose of x-rays is limited to from 1,200 to 1,500 roentgens. The small Treves single cell needles are most satisfactory for this purpose; each needle is loaded with a cell containing either 3.33 or 1.33 mg. of radium. I have found that the optimal dose per needle should not exceed 1.5 millicuries destroyed (200 milligram hours).

The Berven tonsil applicator is an excellent instrument for the topical application of radium to the tonsillar region.[14] This apparatus consists of a dental plate for fixation against the teeth, a pivot-joined piece, the pivots of which fit into the notches of the dental plate and allow movement round a vertical axis, an interlocking hook, a cylindric inner blade of the forceps at the end of which is a radium plate, and an outer blade of the forceps with a pad for pressure against the outside of the cheek. When this instrument is assembled as shown in figure 15, it may be applied to either the right or the left tonsil. The dose and method of treatment are the same as outlined by Berven in his monograph. Atropine sulfate, $\frac{1}{150}$ grain (0.4 mg.), is given hypodermically thirty minutes before the treatment is started. The pharynx is anesthetized by swabbing with a 10 per cent solution of cocaine. Soft warm dental modeling compound is tied on the radium plate, and and impression is made of the region to be treated. After the moulage is cold and firm, the platinum cells, each containing 3.33 mg. of radium, are embedded at a distance of from 0.4 to 0.6 cm. below the surface. As many of these cells as possible are placed side by side within the

14. Berven, Elis G. E.: Malignant Tumors of the Tonsil, Acta radiol., supp. 11, 1931, pp. 1-285.

wax, and the surface is covered with a thin coat of paraffin. The total dose given is from 500 to 1,000 milligram hours. A suitable lead foil protection is affixed to the posterior side of the radium plate. Dental modeling compound is also placed in the dental plate which holds the jaws together when compression is made by the teeth. An outside screw is used to adjust the pressure of the radium applicator against the tonsil and the counterpressure of the outside plate against the

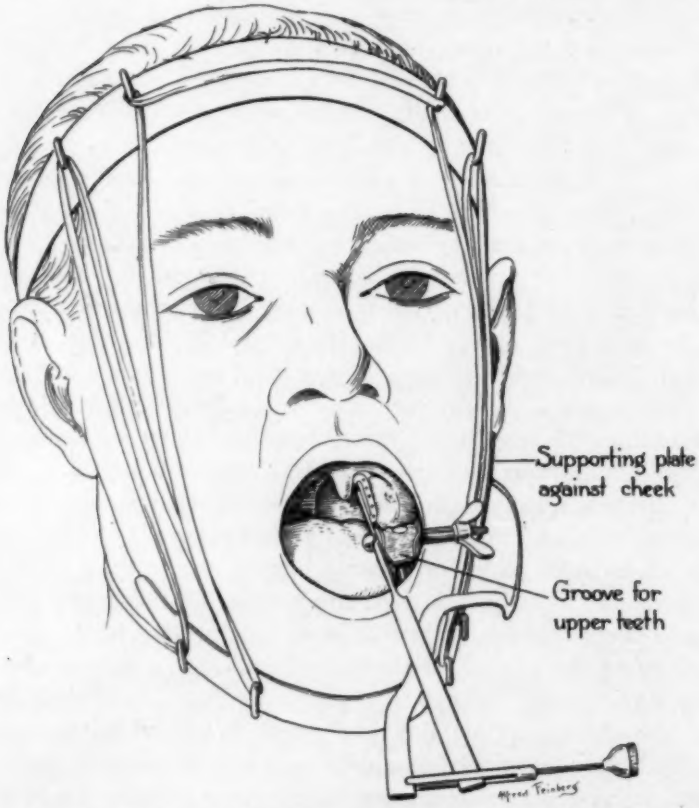

Fig. 15.—The Berven tonsil applicator for the surface irradiation of the tonsillar region. For clarity, the diagram shows the moulage against the tonsil to be small, whereas in practice it covers the entire tonsil.

cheek. It is sometimes necessary to apply this applicator on successive days if the dose is so high that more than ten hours is required for the treatments.

Malignant Tumor of the Antrum or the Superior Maxilla.—Surgical resection is the sole method of treatment for the rare osteosarcoma and chondrosarcoma of the antrum and the superior maxilla. The frequent epidermoid carcinoma of the antrum is treated by a combination of

surgical intervention and irradiation. It is difficult to sterilize the cancer by radium alone because of the danger of radionecrosis, prolonged suppuration and cachexia; hence the radium therapy is always preceded by surgical drainage and épluchage. The x-rays are employed as a routine as a preoperative and supplementary measure. The antral epithelioma grows rapidly, becomes secondarily infected and early invades the nasal fossae, the alveolus, the inferior border of the orbit and the malar bone. There are two stages in the development of carcinoma of the antrum.

In the first stage the carcinoma may invade the alveolar process and even the nasal fossae, especially the anterior ethmoid cells and the

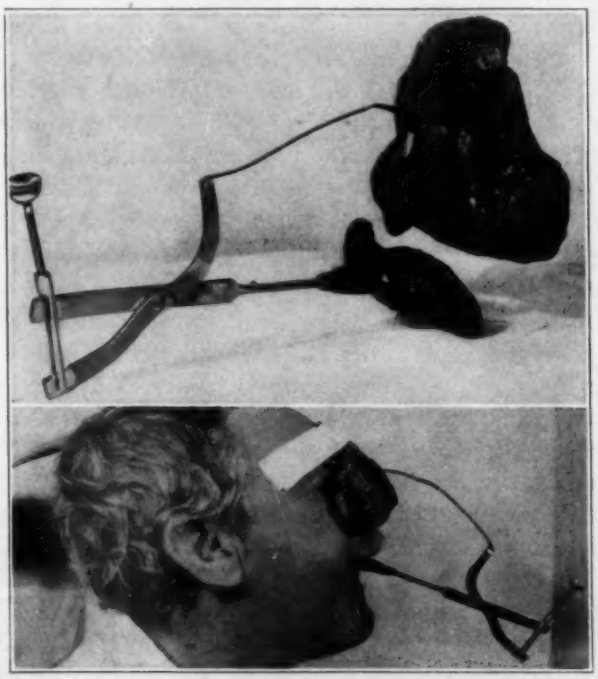

Fig. 16.—The Berven radium applicator used in the treatment of cancer of the palate. The best way for maintaining contact application of a radium moulage in the mouth of an edentulous patient.

internal part of the floor of the orbit. The skin, lymph glands, orbit and palate are not invaded. An incision is made along the nasolabial fold and through the middle of the upper lip to afford sufficient reflexion of the flap to permit exploration of the sinuses and correct placement of the radium tubes or needles. As much of the involved bone is removed as possible, followed by curettage of the cavity. The radium treatment begins immediately after the operation. Radium needles with a platinum filter of 0.5 mm. and a radium content of 3.33 mg. each are packed in

gauze and distributed equidistantly throughout the wound. The average dose is from 20 to 25 millicuries destroyed (from 2,660 to 3,325 milligram hours) given by from ten to fifteen radium needles for from fifty to seventy-five hours. Radium therapy is superior to roentgen therapy in this location because its action is limited, it does not injure the eye, the irradiation is more selective and the skin and hair are less affected. Supplementary roentgen treatment is sometimes given after the radium treatments.[15]

In a more advanced stage, the skin and lymph nodes may be involved as well as the orbit, the temporal fossa, the palate, the nose and even the intracranial cavity. The results from radium therapy and surgical measures are not so good as in the preceding class. Ligation of the external carotid artery is done, followed by a radical resection of bone, including the malar bone and the inferior orbital border, and, if necessary, exenteration of the orbit. The skin should be widely excised if it has been invaded. The prosthesis is not made until cicatrization is complete, which requires from two to six months. Local recurrence is readily detectable, and if it occurs it is accessible because of the character of the operation; such a lesion is treated by radium therapy.

Carcinoma of the Larynx.—Laryngeal carcinoma may be classified according to the site of its origin, e. g., intrinsic on the vocal cords, extrinsic above the vocal cords and subglottic below the vocal cords. Such cancer may also be subdivided into two types by the character of the differentiation. One type, chiefly intrinsic in location, is an epidermoid carcinoma, papillary or infiltrating, which differentiates into sterile squamous sheets and pearls. True prickle cells are found in this tumor. The nuclei frequently disappear entirely. The tumor cells are highly eosinophilic. This epidermoid carcinoma, referred to as the cutaneous type, is relatively radioresistant as compared with the mucous membrane type, which is chiefly extrinsic in origin. In the mucous membrane type, the differentiation is less complete, the pyknotic nuclei are retained in the pearls, prickle cells are lacking and the tumor does not take an intensely pink stain with eosin. The mucous membrane type is more frequently observed on the ventricular fold and is very radiosensitive as a rule.[15] The localization of a vascular, papillary carcinoma on the ventricular fold seems to indicate great radiosensitivity. The classification and histologic grading of the tumor are done by means of biopsy specimens obtained by direct laryngoscopy.

Extrinsic carcinoma of the larynx is treated by external irradiation alone. If the epidermoid carcinoma is of the mucous membrane type

15. Pack, G. T.: The Management of Malignancies of the Antrum, Superior Maxilla, Pharynx and Larynx at the Radium Institute of the University of Paris, Ann. Otol., Rhin. & Laryng. **37**:967, 1928.

of differentiation, regardless of whether it is intrinsic or extrinsic in location, irradiation only is used. The factors used in the roentgen treatment of such a tumor are: 200 kilovolts, 30 milliamperes, a filter of 0.5 mm. of copper and 2.5 mm. of aluminum and a target-skin distance of 60 cm. Although Regaud used four portals, two anterior and two posterior, I have employed only the two anterolateral portals directed to cross-fire at the larynx. A total dose of from 3,000 to 4,200 roentgens is given to each side by the fractionated method with only from 250 to 300 roentgens daily, alternating to each side of the neck. With the foregoing factors, 475 roentgens constitutes a threshold erythema dose for the skin, and 850 roentgens given at one exposure will produce a sharp erythema. Three weeks or so is needed in which to deliver this dose. Certain accidents, such as edema of the larynx, necrosis of the cartilage and intense reaction of the skin or mucous membranes, may occur. They may be prevented in some cases by a preliminary tracheotomy (if necessary), the removal of foci of infection or the removal of cartilage invaded by the carcinoma. The invasion of cartilage may be detected by lateral roentgenograms of the larynx, which are made as a routine. It is extremely difficult to sterilize cancer cells embedded or growing in a cartilaginous base.

Instead of relying exclusively on external irradiation, supplementary intracavitary irradiation may be employed in some cases of intrinsic carcinoma of the larynx. With this combination there is less need for such intensive roentgen treatment. The applicator is modeled after the one designed by Dr. Henry Schmitz, of the Mercy Hospital Institute of Radiation Therapy in Chicago, and later modified by Dr. Walter L. Mattick, of the State Institute for the Study of Malignant Diseases.[16] This applicator is a large intubation tube of the O'Dwyer model, except that the central air space is surrounded by a cylindric chamber containing twelve concentric grooved holes each 1 mm. in diameter. These grooves extend lengthwise of the tube, and each is capable of holding two of the platinum-filtered radium cells placed end to end, so that the source of radiation is well distributed within the larynx. The inner cylinder containing the cells may be made of aluminum, brass or gold, depending on the degree of filtration desired. The lower end of the tube is hard rubber rather than metal in order to lessen the weight of the applicator. The cap which screws over the top of the radium-bearing cylinder is flanged so that it will rest on the glottis and contains a small eye for a thread, which is attached to facilitate its removal. The assembled radium intubation tube is introduced into the larynx, by the usual O'Dwyer technic, where it may be seen in position by inspection with

16. Mattick, W. L.: Some Additions to Our Radiologic Armamentarium in the Treatment of Esophageal and Laryngeal Cancer, New York State J. Med. **33**:863-865 (July 15) 1933.

a laryngeal mirror. The tube is left in place for four hours daily, at which time the patient is mildly narcotized. The quantity of radium employed, i. e., the intensity, varies from 32 mg. (twenty-four cells of 1.33 mg. each) to 80 mg. (twenty-four cells of 3.33 mg. each). The dose varies between 750 and 1,200 milligram hours, depending on the character of the lesion being treated, the degree of filtration used and the quantity of x-radiation employed. Treatments are given daily until the total dose is delivered. This intralaryngeal irradiation never precedes the roentgen treatments. Tracheotomy is not necessarily needed but usually is done until the radium treatments have been completed (fig. 17).

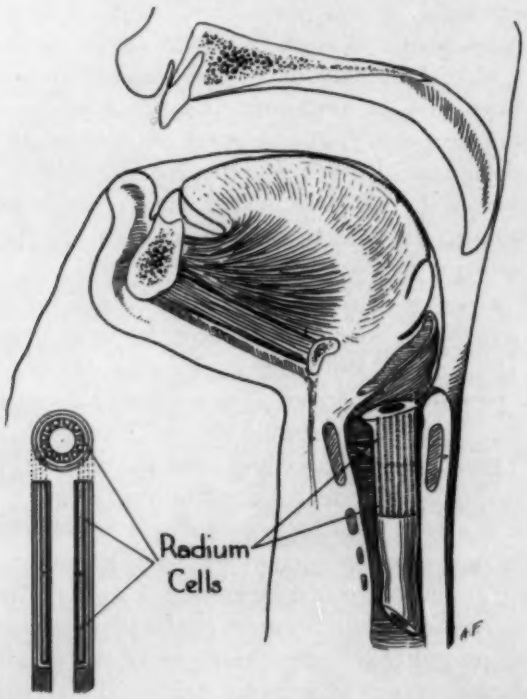

Fig. 17.—Mattick modification of the Schmitz intralaryngeal radium applicator. The O'Dwyer intubation tube is designed to contain two tiers of radium cells arranged concentrically around the lumen. The inner cylinder containing the cells may be made of aluminum, brass or gold, depending on the degree of filtration desired.

An early squamous cell carcinoma on the anterior half of one vocal cord is sometimes dealt with by operative removal. Hemilaryngectomy by the technic of St. Clair Thomson is preferred to such extremes as simple chordectomy or total laryngectomy. The indications for laryngofissure and interstitial radium therapy are becoming less important with the recent marked improvements in external irradiation, although occasionally this procedure has been carried out.

Tumor of the Parotid Gland.—Mixed tumor of the parotid gland is excised surgically. This may be accomplished in practically every case, whether the growth is primary or recurrent, without injury to the facial nerve. The operation is greatly facilitated by preliminary sialography with iodized poppy-seed oil 40 per cent to show the relation of the tumor to the uninvolved parenchyma of the gland. Postoperative external irradiation with radium or roentgen rays induces considerable fibrosis in the gland and is thought to prevent or retard recurrences.

Carcinoma of the parotid gland is treated by a combination of external and interstitial irradiation. High voltage (200 kilovolts) x-rays are applied through a cone directly to the gland and with such a small field that the fractionated doses of from 200 to 250 roentgens may be continued daily until a total dose of from 4,000 to 5,600 roentgens has been delivered. Whenever supplementary interstitial irradiation is deemed necessary, the small single cell radium needles are inserted in gridiron fashion to surround the tumor.

Metastatic Carcinoma in the Cervical Lymph Nodes.—In general, it may be stated that metastatic carcinoma in the cervical lymph nodes is of a higher degree of radioresistance than the original primary intraoral tumor, although there are occasional exceptions to this rule.[12] The radiosensitivity of such a metastatic carcinoma, however, does depend on the character of the primary tumor; e. g., the transitional cell carcinoma and the lympho-epithelioma frequently metastasize to groups of nodes rather than in a single focus, and such metastases are without exception very responsive to irradiation. Carcinoma in the nodes secondary to squamous cell carcinoma of the lip, tongue or cheek can never be controlled by external irradiation alone, either by single intensive treatments or by the application of the Coutard principle of fractionated doses of high voltage x-rays or gamma rays. Carcinoma in such a node forms keratin, is prone to spontaneous degenerative changes, such as liquefaction, and may exhibit desmoplastic fibrotic changes after external irradiation without sterilization of the node. On this account such nodes are treated by the combination of external and interstitial irradiation; the small Treves single cell needles are inserted through the lymph node to deliver a tissue dose in millicuries destroyed based on the size of the node and utilizing the table of dosage requirements previously mentioned. The node is exposed by a small incision through the skin and subcutaneous tissues made with the patient under local anesthesia; the needles are inserted with attached threads to permit removal after delivery of a specified dose. In the case of larger fixed carcinomatous masses in the neck in which the capsules of the nodes have been perforated, transcutaneous puncture is sometimes indicated and larger needles, some containing two platinum cells in tandem, are inserted if

the node is of sufficient size. It is seldom that this supplementary interstitial radium therapy is needed for metastatic carcinoma of the transitional cell or lympho-epithelioma type.

The great problems in the management of these nodes is the consideration of indications and contraindications for a radical or partial cervical dissection and of when to employ radiation therapy in lieu of surgical excision. The best answer to this problem has been furnished by Dr. James J. Duffy:

Indications	Contraindications
1. Metastases limited to one node or group of nodes	1. No apparent metastatic involvement of nodes
2. No perforation of capsule of lymph nodes	2. Perforation of capsule by carcinoma
3. Primary lesion controlled or controllable	3. Primary lesion uncontrolled or uncontrollable
4. Opposite side of neck free from disease	4. Crossed metastasis or bilateral metastasis present
5. Primary lesion limited to one side of oral cavity	5. Extension of primary lesion to or beyond the midline
6. Primary lesion composed of highly differentiated cells	6. Primary lesion composed of undifferentiated cells
7. No distant metastases	7. Distant metastases present
8. Patient in good general health	8. Patient in poor general health or aged
All these indications must be present for dissection.	Any one of these contraindications preclude radical dissection.

A study of this tabulation reveals the interesting fact that the operability of the cervical nodes is determined by the grade of malignancy of the primary lesion as well as by the extent of the metastases. The data are self-explanatory and will not require further comment here.

Prophylactic cervical dissection for intra-oral cancer is never employed. This radical operation is attended by an appreciable mortality and considerable morbidity. Not more than from 10 to 12 per cent of the operations so done will reveal any metastatic foci in the nodes removed; delay in operation in these particular cases would not necessarily be fatal, as many cases are salvaged when recognized metastases are present in the cervical nodes. In an analysis of nine hundred and eighty-three patients with intra-oral cancer admitted to the Memorial Hospital without clinical evidence of metastasis in the cervical nodes, Dr. Duffy found that at the end of three years metastases had not developed in 80 per cent of these patients, which would indicate that in this group 80 per cent of the prophylactic cervical dissections would be unnecessary. It must be realized, however, that all patients with intra-oral carcinoma who do not have evident metastatic involvement in cervical lymph nodes should be examined at frequent intervals so that if such metastases do become apparent they may be treated without harmful delay.

If there are palpable diseased nodes in the neck they are not molested until after the reaction of the intra-oral carcinoma to the radium has sufficiently subsided (a period of about three weeks). Then, if the indications fully warrant it, a unilateral complete block dissection of all the cervical lymphoid tissue is performed. Every lymph node is examined histologically; if carcinoma is found, as is usually the case for the indicated dissection, the neck is irradiated postoperatively and prophylactically by high voltage x-rays or radium therapy at a distance. If no microscopic evidence of carcinoma is discovered in the excised tissues, i. e., if it is inflammatory only, then the neck is not irradiated but carefully watched.

Cancer of the Esophagus.—Preliminary esophagoscopy serves two purposes in cases of esophageal cancer: First, it enables one to obtain a biopsy specimen for histologic grading and determination of the radiosensitivity of the carcinoma, and second, it enables one to measure the distance of the lesion from the incisor teeth. Fluoroscopy also informs one of the extent of the carcinoma and its topographic location, which is recorded at this time by indelible markings on the body anteriorly and posteriorly. Accurate localization of the lesion is necessary in order to insure proper direction of the x-ray beams and the correct placement of radium.

A Janeway gastrostomy, constructed of a tubed pedicled flap from the anterior wall of the stomach and lined by mucosa, is the first step in the treatment. It avoids irritation and lessens infection of the stenosing carcinoma, permits a high caloric diet and proper intake of fluids during irradiation and later enables the retrograde insertion of radium.

With the location and extent of the carcinoma marked anteriorly and posteriorly, four small paramedial ports are selected through which the x-rays are directed to cross-fire at the lesion. These skin portals are the right and left anterior paramedial portals and the right and left posterior paramedial portals. The high voltage x-rays (200 kilovolts peak voltage) are given through a filter of from 0.5 to 1 mm. of copper at 70 cm. target-skin distance. Three hundred roentgens are given to each of the right skin portals, alternating daily with the left skin portals, until from 2,000 to 2,400 roentgens is delivered to each portal. These treatments are completed in from two and a half to three weeks.

Roentgen irradiation is followed in some cases by intracavitary radium therapy. A heavy waxed braided silk thread with a BB shot attached at its end is swallowed by the patient. This string is anchored to the cheek or ear with adhesive tape. A bronchoscope, cystoscope or child's esophagoscope is introduced through the gastrostomy orifice, and the string is grasped and withdrawn on the abdomen. A rubber-enclosed string of radium capsules, from two to four in number, depending on the linear dimension of the cancer, is tied to the string and drawn

into the stomach and then into its proper position in the esophagus. The correct placement of this tandem (the capsules are arranged end to end) is verified by fluoroscopy. Each capsule contains five cells of 3.33 mg. each, or a total of 16.65 mg. of radium. The filter is at least 1 mm. of platinum, as only the very short gamma rays are employed. The dose varies from 1,000 to 1,500 milligram hours (from 8 to 12 millicuries destroyed). Interstitial irradiation of esophageal cancer is contraindicated because of the difficulties and dangers in the correct placement of the seeds and needles, the dose is too caustic and intense, and perforation of the organ with formation of a mediastinal abscess is a possibility in view of the fact that the esophagus does not have a serosal coat.

Cancer of the Stomach.—The treatment of gastric cancer is largely surgical. If the lesion is situated in the distal half of the stomach and is classified as operable, subtotal gastrectomy offers the best opportunity for palliation or even permanent arrest of the disease. The various modifications of the Billroth I operation share in its disadvantages, such as more frequent local recurrence and obstruction. The Billroth II resection and anastomosis are frequently used with the aid of the de Petz sewing clamp. The posterior Polya and anterior Balfour anastomoses are also highly satisfactory. Partial gastrectomy is done occasionally in the presence of distant inoperable metastases, as it is considered a better palliative measure than gastro-enterostomy alone. Resection is occasionally done in two stages in elderly patients with complete pyloric obstruction, when they are considered poor operative risks; the first step is a simple gastro-enterostomy. The second step, or resection, is done in from ten to twenty days after anastomosis has been successfully accomplished. Total gastrectomy should be done if the carcinoma is confined to the stomach and extends into the cardia or fundus, provided the abdominal esophagus is free, mobile and of sufficient length to support an anastomosis. In this operation the esophagus may be sutured either to the duodenal stump or to a jejunal loop. Gastro-enterostomy in itself is not very successful as a palliative measure for gastric cancer; the patient lives to suffer longer. When gastro-enterostomy is supplemented by a simple closure of the involved distal cancer-bearing segment of the stomach, the patient experiences marked relief. Although the cancer is not removed, the proximal part of the stomach is clean, the anorexia disappears, the ulceration and infection of the cancer diminish, the contamination of food is avoided and the danger of later obstruction of the gastro-enterostomy stoma is prevented.

The treatment for the gastric cancer which is classified as inoperable because of fixity, metastases or location (cardia) is palliative radiation therapy. It is well known that carcinoma of the stomach is generally radioresistant. Moreover, the inaccessibility of cancer in this location,

its proximity to the adjacent labile viscera and the necessity of a laparotomy for the insertion of radium have presented other handicaps to successful radiation therapy. Some of these handicaps have been overcome by new technical methods, and some of the cancers, especially those near the cardia, have exhibited various degrees of radiosensitivity. The efforts at radiation therapy have been directed mostly to cancer of the gastric cardia and of the fundus. Gastroscopy and biopsy precede the treatment.

The location and extent of the carcinoma as determined by fluoroscopy are marked on the body surface anteriorly, posteriorly and laterally (left). High voltage x-rays (200 kilovolts) with a filter of 0.5 mm. of copper and at 70 cm. target-skin distance are directed to cross-fire through these portals. A dose of from 250 to 300 roentgens daily is given until each skin port receives a total of from 2,400 to 3,000 roentgens.

External irradiation is occasionally supplemented by interstitial irradiation in the treatment of carcinoma of the cardia. Gold radon seeds are preferable to needles for this technic; however, the latter may be employed if due caution is observed. The cardia and fundus are exposed by a Baudet-Novarro incision running below and parallel to the left costal margin. A costochondral rib flap is either turned up and later replaced and sutured or excised, thereby permitting a more direct approach to the cardia. The small Treves needles containing a single radium cell are inserted obliquely into the cancer so as not to perforate the wall of the stomach. Attached threads for withdrawal are pulled through a cigaret drain, which is removed at the same time as the needles, usually from thirty-six to forty-eight hours later. At the same time a Janeway gastrostomy is usually done. If the carcinoma is bulky and mostly intragastric, other radium needles may be inserted directly into it through an endoscope (bronchoscope, cystoscope or child's esophagoscope) passed through the gastrostomy opening. As much as 40 millicuries destroyed (5,320 millicurie hours) has been delivered interstitially into a gastric cancer. This treatment is still in the experimental stage, although some palliative results have been obtained.

Carcinoma of the Colon.—The usual operation for carcinoma of the cecum, ascending colon or hepatic flexure is done in two stages. First an ileocolostomy is performed, the transverse colon being used, and later resection of the cecum and the ascending colon is carried out. When a carcinoma of the sigmoid flexure, descending colon or splenic flexure is complicated by acute obstruction, a preliminary cecostomy or proximal colostomy is performed, and the resection is done at a later date; the cecostomy serves as a safety valve after resection, and if it is properly done (Witzel technic) the opening will close spon-

taneously. In cases in which there is no obstruction, the Rankin operation of obstructive resection is done, the tumor being removed and the two blind "gun-barrels" being closed for from forty-eight to seventy-two hours. Radiation therapy is seldom indicated for cancer of the colon. Some carcinomas of the cecum are radiosensitive, but irradiation here is reserved for the inoperable or recurrent cancer.

Carcinoma of the Rectum.—Resection of the rectum by any of the approved surgical methods offers the best opportunity for cure of carcinoma of the rectum. However, there are two classes of patients for whom other methods of treatment must be employed, namely, those with inoperable cancers of the rectum and those who refuse operative intervention. Irradiation is not necessarily confined to these groups, as it is often a valuable supplement to surgical treatment as a preoperative or postoperative measure. A rectal cancer histologically classified as of grade 3 or 4, on the basis of the differentiation receives a pelvic cycle of high voltage x-rays directed through four skin portals, two anterior and two posterior, to cross-fire at the rectum; fractionated doses of 300 roentgens are given daily to alternate portals until 2,000 or 2,400 roentgens is given to each area. The effect of these treatments is seen in the great diminution in the size of the tumor, its increased mobility, the subsidence in the degree of infection and the general improvement of the patient. Resection of the rectum is then carried out from four to six weeks later.

A carcinoma situated in the rectal ampulla and classified as operable may be treated in the following sequence: preliminary treatment with high voltage x-rays, then colostomy followed by interstitial irradiation with radium element needles, and finally perineal resection.[17] Interstitial irradiation prior to surgical resection is seldom used except for the infiltrating carcinoma which is classified histologically as grade 2. External irradiation is never used prophylactically for postoperative treatment; it is employed only when the surgeon considers the resection incomplete or a local recurrence has actually developed.

The technic for the irradiation of the rectal cancer will be summarized briefly. After completion of the roentgen treatments, as previously described, the main reliance must be placed on interstitial irradiation. Intracavitary irradiation with a tandem of radium capsules or the surface application of radium within the rectum is seldom indicated except when used to enlarge the lumen through a stenosing carcinoma.

A most necessary adjunct to successful radium therapy is colostomy, performed with a short distal segment in order to facilitate retrograde

17. Binkley, G. E.: Colostomy, Radiation Therapy and Perineal Resection for Cancer of the Rectum, J. A. M. A. **99**:1592-1596 (Nov. 5) 1932.

sigmoidoscopy. Other advantages afforded by the colostomy are: the short circuiting of the fecal current and avoidance of contamination of the cancer during treatment, subsidence of infection in the cancer and facility in irrigation of the cancer bearing segment in preparation for the introduction of radium.

Sheath needles containing one or two of the platinum radium cells are inserted into and through the base of the tumor through the anus, either by guidance along a palpating finger when the cancer is situated low or through a proctoscope under direct vision. The needles are placed usually in the longitudinal axis of the rectum and are distributed circumferentially. Additional needles may be inserted through small

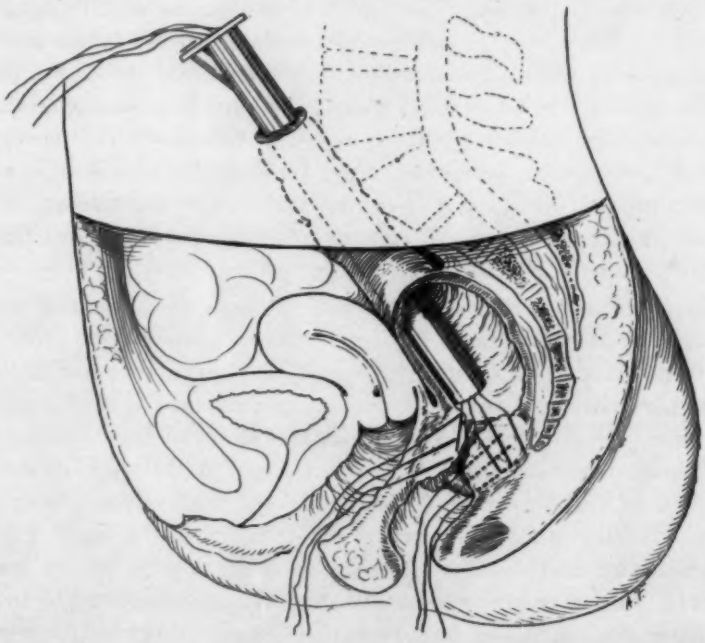

Fig. 18.—Method of interstitial radium therapy for rectal cancer in the female. The single cell radium needle is inserted through the anal orifice and the posterior vaginal wall, and a sigmoidoscope is passed in retrograde direction through the short lower limb produced by a loop colostomy.

puncture wounds in the perineal and postanal regions when the carcinoma infiltrates anteriorly or posteriorly, respectively. The superior pole of the cancer is best approached through a sigmoidoscope passed downward through the inferior stoma of the double-barreled colostomy opening. Through this instrument additional radium needles may be inserted from above (fig. 18).

In females, cancer situated in the anterior wall of the lower part of the rectum may also be treated by the introduction of these needles

into the tumor through the posterior vaginal wall. This placement can be done accurately if the index finger of the left hand is inserted in the rectum to guide the direction of the needles. Overdosage in this location may result in a rectovaginal fistula. A longitudinal incision may be made posterior to the anus and extending above the coccyx, which may be removed to afford better exposure of the ischiorectal fossa. Through this opening additional radium needles are placed around the cancerous segment of the rectum in the manner of a barrage. This procedure has been employed by Sir Charles Gordon Watson.

Double waxed silk threads are attached to the needles for their removal, which is usually done on the third to the fifth day. The total dose depends on the size and extent of the tumor and its local characteristics. The dose is seldom greater than 50 millicuries destroyed. In one instance the radium needles were introduced through a posterosuperior proctotomy; a vertical incision was made posterior to the anus and above the sphincter, which was not harmed. The coccyx and terminal two sacral vertebrae were removed, exposing the rectum. The rectum was then incised longitudinally, and radium was inserted into the cancer under direct vision. This procedure is feasible only when the tumor is situated high in the rectum.

Tumor of the Kidney or Adrenal Gland.—Any operable renal or adrenal neoplasm is treated by nephrectomy followed by prophylactic high voltage roentgen treatment. Inoperable, recurrent and metastatic hypernephroma, renal papillary adenocarcinoma and epithelioma of the renal pelvis are also treated by fractionated doses of high voltage x-rays but without much success, as the few tumors of this type treated have proved to be radioresistant. The embryonal adenomyosarcoma of the kidney (Wilm's tumor) occurring in children has a high degree of radiosensitivity and usually regresses completely after heavy roentgen treatment; this intensive preoperative irradiation is followed by nephrectomy after the regression has reached its limit; otherwise recurrence is the rule (Dean and Pack[18]).

Benign or Malignant Tumor of the Urinary Bladder.—Whenever one or two benign papillomas of the bladder can be visualized through the cystoscope, it may be possible to remove them by an endotherm snare, which procedure is always followed by the insertion of gold radon seeds into the base of the tumor, after the method originated by Barringer.[19] Papillary carcinoma also may be treated through the urethra

18. Dean, A. L., Jr., and Pack, G. T.: Embryonal Adenocarcinoma of the Kidney, J. A. M. A. **98**:10-17 (Jan. 2) 1932.

19. Barringer, B. S.: The Past and Present in Genito-Urinary Carcinoma, Am. J. Surg. **23**:438-441, 1934.

by this method, if the base of the tumor is not larger than 1.5 cm. in diameter. The dosage for these treatments has been determined by Dean and Quimby [20]; gold radon seeds of 2 millicuries each are buried to the depth of 1 cm. and placed 1 cm. apart.

The papillary carcinoma, regardless of size, and the flat infiltrating carcinoma are exposed by suprapubic cystotomy for the more accurate placement of radium foci. Dean and Quimby have shown by experiments that a larger number of relatively weak sources of radiation are preferable to fewer strong radium foci. Hollow sheath needles are accurately inserted into the base of the tumor through the suprapubic wound; attached threads for the removal of these needles are drawn through the suprapubic wound and anchored to the abdominal wall. The threads are impregnated with yellow wax so that they will not become weak and rotten while constantly immersed in urine. These single cell needles are placed at intervals of 1 cm. The following scheme of dosage is employed. Needles containing 3.33 mg. cells give a dose of 2 millicuries destroyed (266 milligram hours) per square centimeter of tumor base if left in situ for eighty hours. Sixty hours of interstitial radiation with needles of this strength will deliver a dose of 1.5 millicuries destroyed (200 milligram hours) per square centimeter of tumor treated. If the needles contain the cells of less radium content—the 1.33 mg. cells—the duration of treatment must be one hundred hours in order to give a dose of 1 millicurie destroyed per square centimeter; this dose is not always cancerocidal.

High voltage roentgen treatment is chiefly employed as a palliative measure for inoperable and recurrent carcinoma of the bladder. It is more successful for papillary carcinoma and may be used postoperatively as a supplement to interstitial irradiation. At a distance of 100 cm. and with a low daily dose of only 100 roentgens, Ferguson in a series of cases has successfully controlled papillomatosis of the bladder, ureter and kidney.

Carcinoma of the Prostate.—Prostatic cancer is first treated by a pelvic cycle of high voltage x-rays. Cancer of the prostate in the advanced stage with demonstrable metastases is treated solely by fractionated doses of x-rays, from 250 to 300 roentgens being given daily to one of the four pelvic portals and alternated daily until 2,000 or 2,400 roentgens are delivered. The target-skin distance is 70 cm., the filter 0.5 mm. of copper and the milliamperage 20, and the beams of radiation are directed to cross-fire at the prostate. The entire cycle is seldom completed in less than one month. When roentgen therapy is to be followed by interstitial irradiation, only four exposures of 750

20. Dean, A. L., Jr., and Quimby, E. H.: Radiation Therapy of Carcinoma of the Bladder, Surg., Gynec. & Obst. **53**:89-96, 1931.

roentgens each are given to the pelvic portals. As Barringer has found that the average carcinoma of the prostate requires 10 skin erythema units as a tissue dose delivered to all parts of the tumor in order to effect its complete destruction, roentgen therapy must be supplemented by interstitial irradiation.[19]

Interstitial irradiation of the prostate is accomplished through two ports of entry. With the patient under sacral anesthesia, a stab wound is made in the perineum, and through this opening from eight to ten radium bearing needles (contents either 1.33 or 3.33 mg.) are introduced into the prostate. These needles are affixed in the hollow-cupped ends of long-handled rods, which facilitate their introduction through the perineum and are easily dislodged when in the prostate, leaving the needles in place with strings attached for withdrawal. They are directed and accurately placed with two fingers of the other hand in the rectum. Other single cell needles are inserted through the incision made for a suprapubic cystotomy. The base of the bladder is exposed by the assistant. The operator stands on the patient's left and with two fingers of his left hand in the rectum inserts the needles through the suprapubic wound into the prostate with the right hand. The dose depends on the size of the prostate; it seldom totals more than 50 millicuries destroyed (6,650 milligram hours) and is computed at from 1 to 2 millicuries destroyed per cubic centimeter of tissue irradiated.

Epithelioma of the Penis.—When a penile cancer is early, superficial and situated on the prepuce, circumcision is done, followed by topical radium therapy. Radium therapy by surface application is also suitable for early cancer of the glans penis. A square, rectangular or round plaque (as previously described) is selected, according to the surface area to be irradiated. The radium-skin distance, filter, intensity and dosage are the same as for epithelioma of the skin. Or an individual wax moulage may be molded for each individual patient and platinum cells of 3.33 mg. content embedded at a depth of from 0.25 to 0.5 cm. to give a dose of from 0.8 to 3 millicuries destroyed (from 100 to 400 milligram hours) per square centimeter of skin area. The glans and preputial skin are quite sensitive to irradiation and will not tolerate interstitial irradiation without danger of radionecrosis. Partial or radical amputation may be necessary for more advanced epithelioma, followed by prophylactic external irradiation of both groins. If the inguinal lymph nodes are involved by metastatic carcinoma, bilateral inguinal dissection is done as a second stage operation. The inguinal dissection should be done prior to external radium therapy or high voltage roentgen therapy; otherwise tissue changes due to radiation delay the healing of the inguinal wounds. In Barringer's wide experience, involvement of the inguinal lymph nodes by carcinoma occurs in

only 40 per cent of the cases of penile cancer, on which account routine prophylactic dissection of the groin has not been adopted. An alternative to dissection of the groin is exposure of the carcinomatous nodes and implantation of one cell radium needles.[19]

Teratoma of the Testis.—The malignant testicular neoplasm is treated by a combination of external irradiation followed by orchidectomy. The initial response of the tumor, as judged by the rapidity and extent of reduction in size, indicates to some degree the histologic type of tumor. Although it is posible to sterilize the embryonal carcinoma and seminoma by external irradiation, one may never rely on that method

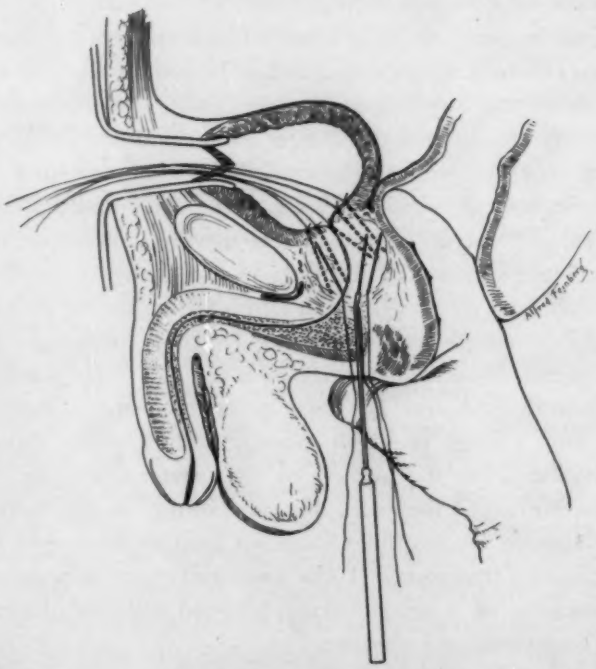

Fig. 19.—Method of interstitial radium therapy for prostatic cancer. The single cell or two cell radium sheath needles are introduced into the prostate gland through a suprapubic cystotomy and the perineum. The insertion and guidance of the direction of the needles inserted through the perineum are aided greatly by the insertion of a forefinger in the rectum.

for the control of the tumor. The advantages of postradiation orchidectomy are: first, it prevents overirradiation to the opposite testicle; second, it removes all the local neoplasm, including the radioresistant portions of the adult teratomas, and, finally, it enables the pathologist to classify the tumor, which is of great aid in judging the few methods of treatment. The abdominal metastases are treated by external irradiation only, roentgen rays of 200 kilovolts, a 0.5 to 1 mm. copper filter

and a target-skin distance of from 70 to 100 mm. being used for a large skin port both anteriorly and posteriorly and fractionated doses of 300 roentgens being given daily to alternating areas until a total of from 2,000 to 3,000 roentgens is given.

The most important contribution to the successful management of this tumor is the estimation of a follicle-stimulating principle in the urine as perfected by Ferguson. The quantitative estimation of this principle in the urine may not only indicate the embryonal character, the degree of malignancy and consequently the response to radiation of the primary tumor, but may serve to detect abdominal metastases or recurrences long before these lesions are palpable.

Malignant Tumors of the Vulva.—The treatment of vulvar epithelioma is essentially a surgical problem. Radiation therapy is followed by immediate edema, swelling and marked inflammatory reaction accompanied by extreme pain and the danger of late radionecrosis. The moist vulvar skin does not tolerate external irradiation well, and the tissues are too delicate and sensitive to permit of interstitial irradiation. Furthermore, the vulvar epithelioma is usually a radioresistant cancer with a histologic grading of 1 or 2. Vulvectomy is usually the best procedure, followed by prophylactic external irradiation of both groins. If the inguinal lymph nodes are involved by metastatic carcinoma, bilateral inguinal dissection is done as a second stage operation. The inguinal dissection should be done prior to heavy external radium therapy or high voltage roentgen therapy, otherwise the tissue changes due to radiation delay the healing of the inguinal wounds. In a few cases, I have implanted the small one cell radium needles in the exposed inguinal or femoral nodes, but I have not been impressed by the results of this method of treatment. I am more and more impressed with the ultimate necessity of a second stage bilateral inguinal dissection even though no metastases are evident.

Carcinoma of the Cervix.—The majority of carcinomas of the cervix (97 per cent) are of the epidermoid type, histologically graded as squamous, plexiform and anaplastic; the other 3 per cent are adenocarcinomas, though some of these may have originated in the corpus. The selection of the radiotherapeutic procedure depends more on the stage or extent than on the histologic structure of the tumor. In this consideration the classification adopted is the one formulated by the Radiological Subdivision of the Cancer Commission of the League of Nations.

Stage 1: The carcinoma is limited entirely to the cervix. The uterus is movable, and no paracervical induration is detectable.

Stage 2: The carcinoma has extended to involve part of the vaginal fornices slightly, with or without some induration of the paracervical tissues. The uterus has some degree of mobility, and the stage is one of borderline operability.

Stage 3: The uterus is partly or completely fixed, with induration of the parametrium on one or on both sides, or there is involvement of a considerable portion of the vagina, though the uterus is movable.

Stage 4: The cancer has invaded adjacent viscera, involves most of the vagina and has metastasized beyond control. It is incurable.

The radical panhysterectomy (Wertheim) can be done only for cervical cancer in stage 1, but even in this early stage the results of treatment are not better than when radiation therapy is employed. There are few gynecological surgeons trained to do this formidable operation, of which the morbidity and mortality are considerable; on the other hand, radiation therapy is so well planned, standardized, easy to execute and free from danger that it permits of more general usage. Surgical treatment is absolutely indicated in those cases of cancer of the cervix in which radium therapy is inefficient or dangerous. It is considered to be inefficient when the cancer is known to be radioresistant, as when an operable cancer has been treated by radium therapy and has proved radioresistant, so that more irradiation might cause radionecrosis. In such a case hysterectomy is the last possible method of treatment. Radium therapy is often insufficient for a cancer which is very feebly radiosensitive, such as an adenocarcinoma. The uterovaginal method of applying radium is inefficient when a malformation of the uterus (atresia, irreducible flexion) or of the vagina (congenital or cicatricial stenosis) will not permit the typical and correct technic. If the cancer is operable, it is best to practice hysterectomy and reserve radiation therapy (x-rays and external foci of radium) as a resource against recurrence. Radiation therapy is dangerous when the cancer is complicated by adnexal inflammation. One may attempt to suppress the inflammatory process and, if sufficiently successful, may later attempt surgical removal followed by external irradiation.[21] Before either radium or roentgen therapy is given, the possibility of latent or chronic pelvic inflammatory disease should be ruled out. Irradiation under such circumstances is fraught with many dangerous complications, such as salpingitis, pelvic phlegmon, peritonitis and septicemia. These accidents seldom occur if the vaginal flora is free from streptococci.

A cervical cancer in stage 4 is not suitable for any form of treatment. All cervical lesions in stages 1, 2 and 3 are treated by irradia-

21. Pack, G. T.: The Management of Uterine Malignancies at the Radium Institute of the University of Paris, South. M. J. **21**:505-515, 1928.

tion alone; the dose and technic are essentially the same for all three stages, as the maximal doses of radiation are always employed.

The greatest recent advances in the treatment of cervical cancer have followed the adoption of some type of fractionated prolonged roentgen therapy, modified from the Coutard technic. This principle includes such factors as an increased target-skin distance (of 70, 90 or even 100 cm.), heavier filtration (1 mm. of copper) and daily repeated small doses (from 200 to 250 roentgens) to multiple pelvic portals (from 6 to 8) over a period of three weeks. Several ports are treated daily, alternating around the pelvis until each port receives from 1,800 to 2,100 roentgens. These measures have enabled the roentgenologist to give a larger depth or tissue dose to the cancer and to realize to the utmost the difference in radiosensitivity of the cancer and the intervening normal tissues, on which successful radiation therapy depends. The bulky, exophytic, papillary cancer may regress almost completely after the cycle of roentgen treatments so that the subsequent and supplementary radium therapy is considerably simplified. If it does not diminish greatly, it is my practice to excise it by means of an insulated endotherm loop snare. This avascular procedure has certain advantages to commend it; it removes the infected sloughing portion of the tumor; it permits the intra-uterine radium tandem to be placed in closer approximation to the base of the tumor and thus delivers a more effective dose, and finally it lessens the dose of intravaginal irradiation to be directed against the cervix.

The vaginal radium applicator to fit against the cervix to irradiate it and the parametrium is known as the Curie colpostat.[22] It consists of two corks mounted on a flexible steel strip covered by rubber tubing. Each cork is 1.5 cm. broad and 2.5 cm. long, so that with the radium-containing capsule within its interior more than 0.5 cm. wall of cork is left on either side. The ends of the corks are sealed with plugs. The apparatus is introduced into the vaginal fornices without anesthesia and is so directed that only the ends of the capsules are toward the rectum and bladder, the broad radiating surfaces facing the cervix and parametrial tissues. Additional radium-bearing corks may be adjusted within the concavity of the colpostat. A total dose of from 2,000 to 3,000 milligram hours is given with this applicator in addition to the intrauterine dose. The filter is the equivalent of 1 mm. of platinum. If the uterine canal is impermeable, the treatment is made at two successive times, the vaginal applicator first (colpostat) and the uterine applicator later, after regression of the neoplasm has disengaged the canal. With only a small quantity of radium available these treatments are necessarily given in succession rather than simultaneously (fig. 20).

22. Regaud, C.: Traitement des cancers du col de l'utérus par les radiations, Cong. de la Soc. internat. de chir., Rep. **1**:35-146, 1926.

The platinum capsules used in the colpostat have a wall thickness of 0.3 mm. of platinum. Each capsule is loaded with four of the unit cells of 3.33 mg. radium content each. This brings the total filtration value to 0.5 mm. of platinum. The platinum capsule or tube is now introduced into a heavy brass capsule of such wall thickness as to add an additional value of 0.5 mm. of platinum, making a total filtration of 1 mm. of platinum. If three capsules are employed, each containing four cells, or 13.3 mg. of radium, the total content of the colpostat would be 40 mg. With this intensity, a dose of 3,000 milligram hours would require seventy-five hours.

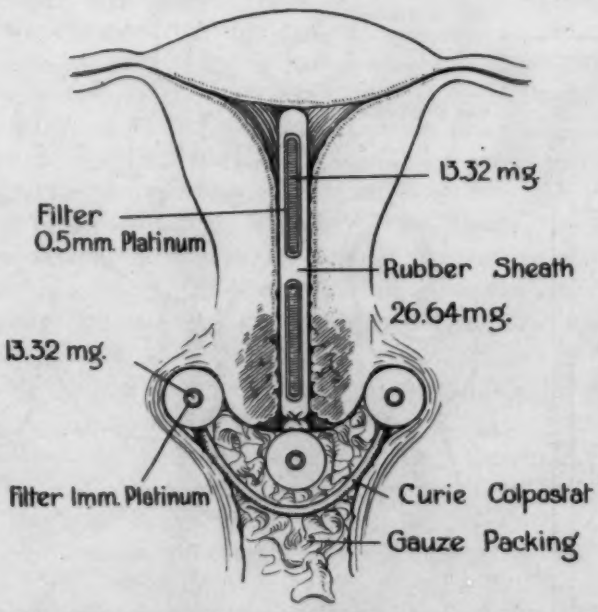

Fig. 20.—Distribution of radium in the treatment of carcinoma of the cervix uteri. In the uterine tandem the cervical capsule has twice as large a content of radium as the one in the fundus. The radium-bearing capsules in the colpostat have twice the filtration that is used in the uterine tandem.

In lieu of the Curie colpostat, the vaginal bomb as used by Healy at the Memorial Hospital may be substituted. This instrument (fig. 20) is applied against the cervix and toward the parametrium on each side. Its position is maintained by an adjustable upright standard attached to a "bomb board" with knee rests, which may be placed in the patient's bed. All the available radium (130 mg. in this instance) in platinum cells is placed within the cavity of the bomb. The filter consists of 0.2 mm. of platinum, 1 mm. of brass and 1 mm. of steel. The bomb has a circular surface with a diameter of 1½ inches (3.8 cm.). The dose is from 1,200 to 2,500 milligram hours, depending on whether

the application is in a single direction, e. g., central, or toward the parametrium on each side. This applicator can seldom be tolerated for more than five hours daily, as it is introduced without anesthesia. The treatment is completed in from two to four days (fig. 21).

The last and most important step in the treatment of carcinoma of the cervix is the insertion of an intra-uterine (and intracervical) tandem of radium capsules. The depth of the uterine cavity is measured by a sound in order to plan the length of the rubber tube containing the

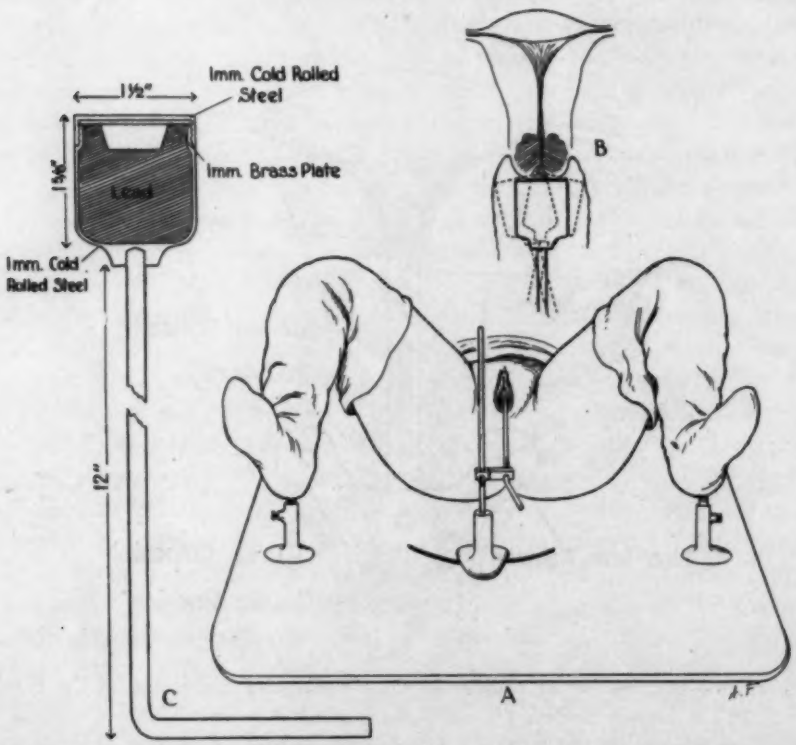

Fig. 21.—Radium bomb (*C*) for vaginal irradiation directed toward the cervix and parametria (*B*). In *A* the patient is shown in bed, resting on a specially designed board, with knee rests and adjustable bomb support, which permits the direction of the bomb to the center, right or left of the cervix. This apparatus is an exact model of the type used by Healy, of the Memorial Hospital.

radium. It is most essential for the entire length of the uterine cavity to be filled with radium capsules in tandem, otherwise the fundus will not scar and contract later, in which event pyometra may result. This tandem of radium capsules may be introduced in many patients without the use of an anesthetic if graduated Hegar sounds are used for the cervical dilatation. The filter of the intra-uterine capsules is 0.5 mm. of platinum. There are usually two capsules, a lower one in the cervical

canal and an upper one in the fundal cavity. The cervical capsule or tube contains eight of the unit cells of 3.33 mg. each (26.64 mg.), and the capsule or screen in the uterine cavity contains only four of these cells (13.32 mg.). Thus it is planned for the cervix to receive twice the dose that is given to the corpus uteri (fig. 20).

The radium within the uterus and vagina may require from three to five days in order to furnish the necessary sterilizing dose, but each morning these applicators are removed and sterilized while the patient is receiving a douche and then are reintroduced. The end-results in terms of five year cures are approximately the same whether the radium therapy is given intensively in from twelve to eighteen hours or continuously for five days, but the pliability and integrity of the vaginal vault are immeasurably better with the longer treatment. The intra-uterine dose is from 3,000 to 3,600 milligram hours; the latter dose is given only when the cavity of the body of the uterus is so long as to require two of the weaker radium capsules in addition to the more intensive irradiation within the cervical canal. The cautious radiologist will attempt to prevent undue irritation of the bladder and rectum by packing the anterior and posterior vaginal fornices tightly while the radium is in situ. This pushes these labile organs as far away as possible from the source of radiation and tends to prevent ulceration and the formation of fistulas.

Cancer of the Body of the Uterus.—Once carcinoma of the body of the uterus is diagnosed, the decision as to the method of treatment depends not only on the stage of the disease, i. e., technically operable or inoperable, but also on the histologic grade of the neoplasm. The anaplastic corporeal cancer of grade 4 is treated solely by radiation therapy even when in an operable stage. Cancers of the corpus of grades 1 to 3 are treated by radical panhysterectomy after intra-uterine radium therapy; roentgen irradiation in these cases is reserved for post-operative use.

The technic for irradiation of the inoperable cancer and the operable cancer of grade 4 is as follows: Preliminary high voltage roentgen therapy is given to four pelvic ports (sometimes six, to include lateral fields), the fractionated principle being employed, as for carcinoma of the cervix. An occasional disadvantage after such treatment is that the uterine canal may be so small that the subsequent introduction of radium is difficult. Emphasis is placed on the intra-uterine tandem of radium capsules. The filter of these capsules is the equivalent of 0.5 mm. of platinum (0.3 mm. of wall and 0.2 mm. for the enclosed platinum cells). There are usually three capsules, each containing four of the unit cells of 3.33 mg. each (13.32 mg.). The intra-uterine dose is from 3,600 to 4,000 milligram hours, more commonly the first.

Six weeks later a curettage is done for diagnostic purposes, and if viable carcinoma is found in the material obtained intra-uterine radium therapy is repeated, a smaller dose being used. If panhysterectomy is to be done, the operation is delayed until six weeks have elapsed after the completion of the preoperative irradiation.

Malignant Tumor of the Ovary.—Surgical removal of a tumor of the ovary is indicated because the clinician cannot always tell preoperatively whether the tumor is benign or malignant. The accepted treatment for malignant ovarian tumor is panhysterectomy. In some cases it has been thought wise to do a bilateral salpingo-oöphorectomy, the uterus being left in place to serve as a holder for radium. If the panhysterectomy removes all the clinical evidence of cancer, the patient nevertheless receives a prophylactic pelvic cycle of high voltage roentgen rays, consisting of 300 roentgens daily alternating to each of four or six ports until 2,000 roentgens are delivered to each field. A target-skin distance of 70 cm. is used. If peritoneal carcinosis is found at laparotomy, the primary tumor and the opposite ovary are removed if possible, as the carcinomatous implants and metastases have been known to disappear or regress or become inactive at the cessation of ovarian stimulation. If the ovarian carcinoma is manifestly inoperable at the time of diagnosis, roentgen therapy should be given. These treatments may cause the tumor to regress and become sufficiently mobile to permit later surgical removal, possibly resulting in better palliation. Healy emphasized the importance of irradiating the abdominal scar in all of these cases because of the danger of implants if rémoval of the malignant tumor is done.

For inoperable ovarian carcinoma additional radiation may be given by an intra-uterine tandem of three radium capsules for a dose of 4,000 milligram hours. The filter of these capsules is equivalent to 1 mm. of platinum, which affords a shorter and more penetrating gamma ray than is customarily used in the case of uterine cancer. If external irradiation is relied on as a sole method of treatment, the dose in roentgens delivered to each skin port by the fractionated method is increased to as high as 2,500 roentgens.

Cancer of the Breast.—The treatment of choice for operable carcinoma of the breast is radical amputation. Radical mastectomy is preceded by roentgen irradiation only when the carcinoma is on the borderline of operability; when the degree of malignancy—as judged by the clinical index—is high, and in young women when metastases are present in axillary nodes. This operation is one of the most successful in the field of cancer surgery; local recurrence develops in less than 10 per cent of cases, and then usually when the operation was ill chosen. The failure of the operation to cure the patient is usually due not to local recurrences but to distant metastases. Postoperative roentgen therapy is advised for

use as a routine, for it is believed to decrease the incidence or at least to delay the appearance of local recurrences. The methods of radiation therapy are not exact enough as yet to justify their routine substitution for radical mastectomy. Primary operable mammary cancer is treated by irradiation alone under two conditions: (*a*) when operation is contraindicated by the poor general condition of the patient and (*b*) when operation is flatly refused. Every recurrent and inoperable carcinoma is treated by irradiation, usually a combination of roentgen rays and interstitial radium. The criteria of inoperability are based on the presence of any one of the following conditions: inflammatory carcinoma, carcinoma in the lactating breast (carcinoma mastitoides), fixation of tumor, fixation of axillary nodes, metastatic involvement of supraclavicular nodes or nodes in the opposite axilla, invasion of the opposite breast, marked extension into the skin and metastasis to the lungs, liver, bones, etc.

Carcinoma situated in the breast has certain physical advantages for the treatment by irradiation.[23] The mammary gland is superficial enough so that any tumor in its depth may receive a considerable percentage of the energy from external sources of radiation. The accessibility of the breast permits a reasonably correct measurement of the tumor, an accurate estimation of the dosage and the proper implantation of radioactive foci. The reactionary phenomena after irradiation of the breast are of little moment and are seldom complicated by sloughing and infection. The loss of mammary function is unimportant to patients with carcinoma of the breast, since their average age is slightly over 50 years.

Opposed to these advantages are certain undeniable handicaps to successful irradiation of cancer of the breast. Mammary cancer is generally relatively radioresistant.[24] The thick fat envelop of the breast is an extremely poor reactive tissue bed, which contributes little in the way of productive inflammation and fibrosis toward the destruction of carcinoma by irradiation. The delicate and moist skin of the axilla and sulcus of the breast will not tolerate much external irradiation. Cancer of the breasts in many cases metastasizes widely before any treatment is instituted.

Previous communications from the Memorial Hospital presented in detail a new method of treating mammary cancer by measured tissue doses of radiation, delivered from external sources (roentgen rays) and by interstitial deposition of gold radon seeds.[23] The cancerocidal

23. Lee, B. J.; Pack, G. T.; Quimby, E. H., and Stewart, F. W.: Irradiation of Mammary Cancer with Special Reference to Measured Tissue Dosage, Arch. Surg. **24**:339-410 (March) 1932.

24. Stewart, F. W.: Radiosensitivity of Tumors, Arch. Surg. **27**:979-1064 (Dec.) 1933.

dose by physical and clinical experimentation has been determined as 10 threshold erythema doses. The depth dose which reaches the tumor from external sources of radiation was added to the interstitial dose. The accurate placement of interstitial radium in proper dosage can effect complete destruction of the mammary cancer, as has been demonstrated by clinical experimentation and subsequent microscopic study of the breast after amputation.[25]

The entire glandular system of the breast is condemned in certain varieties of mammary cancer. Diffuse ductal cancer involves the ducts in almost every lobule of the breast. Every duct is a potential site of cancer origin in the case of Paget's disease of the nipple. Even the localized carcinoma is accompanied by precancerous changes in the ducts of other lobules. I have occasionally seen multiple discrete cancers in the same breast; their multicentric origin can be attributed to a common underlying predisposition to cancer existent throughout the entire breast. In the majority of cases of cancer of the breast, infiltration of cancer cells extends beyond the palpable limits of the tumor. In such instances the palpable tumor may be completely devitalized by accurate interstitial irradiation, yet recurrence may appear later in a part of the breast peripheral to the original tumor. The factors enumerated above suggest a requirement of the utmost importance. The breast and the adjoining regions of lymphatic drainage must receive diffuse rather than focal irradiation, and the dose must be lethal for cancer cells in any environment.

If a mammary cancer is to be treated solely by radiation therapy, the following technic is employed. After confirmation of the diagnosis by aspiration biopsy, the breast, axilla and supraclavicular space are treated by high voltage roentgen therapy. The five skin portals commonly used are the median side of the breast, the lateral side of the breast, the axilla direct, the axilla posterior and the supraclavicular space, the latter field including the superior part of the breast and the anterior axilla. The beam is directed tangentially to the wall of the chest to avoid as far as possible the danger of late pulmonary fibrosis. Two fields are treated daily at 50 cm. target-skin distance with doses of 250 roentgens each. Treatments are alternated daily until each field receives from 1,500 to 1,750 roentgens. The external irradiation is followed immediately by the insertion of radium needles.

The breast and axilla are prepared as for any surgical operation. Anesthesia is induced and maintained as a rule by the intravenous administration of the sodium salt of normomethylcyclohexenylmethylmalonylurea. The introduction of the radium needles is facilitated by

25. Lee, B. J., and Pack, G. T.: Irradiation of Mammary Cancer with Special Reference to Measured Tissue Dosage, Acta radiol. **12**:416-454, 1931.

puncturing the skin with a small pointed knife (no. 11 Bard-Parker blade). The dose to be given by interstitial radium therapy is calculated by subtracting the tissue dose delivered by the roentgen rays from the known cancerocidal dose of from 6 to 10 threshold erythema doses. The number of millicuries destroyed or milligram hours may then be ascertained by consulting table 4. The size and position of the tumor as well as the relative size of the breast influence the arrangement and distribution of the needles. The radial arrangement of Keynes is suitable for the small cancer which is centrally situated.[26] A larger tumor necessitates the placement of the needles in a series of parallel rows or even in gridiron formation.[27] The needles surround the tumor in most instances, as there is some suspicion that insertion into the carcinoma

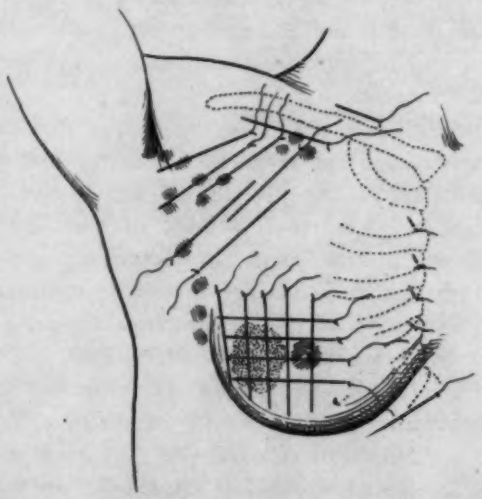

Fig. 22.—Distribution of radium-bearing needles in the breast, axilla, supraclavicular space, epigastrium and parasternal intercostal spaces. The sheath needles vary in length and contain from one to four of the small radium cells placed end to end.

itself involves the risk of transplanting or disseminating the cancer. As the main lymphatic channels run deep to the breast in the pectoral fascia, the greatest concentration of interstitial irradiation is rightly in this plane; this also avoids excessive irradiation to the skin, a complication which may follow the too superficial implantation of radium needles. Keynes has always stressed the point that a gap of untreated breast should not be left between the tumor and the anterior fold of the axilla.

26. Keynes, G.: (*a*) The Treatment of Primary Carcinoma of the Breast with Radium, Acta radiol. **10**:393-402, 1929; (*b*) Radium Treatment of Carcinoma of the Breast, Lancet **1**:439-442 (March 1) 1930.

27. Pack, G. T.: The Interstitial Use of Gold Filtered Radon Transfixion Tubes in the Treatment of Mammary Cancer, Am. J. Roentgenol. **27**:532-546, 1932.

The total dose in the breast varies from 40 to 80 millicuries destroyed. The needles may be of the long sheath variety, containing four of the platinum cells in tandem, or shorter needles holding only two radium cells may be used.

In the axilla, the radium needles are inserted fanwise in order to afford diffuse and accurate irradiation to the axillary contents. They are introduced from below upward or downward from the infraclavicular region, care being taken to avoid the neurovascular bundle at the apex of the axilla. The insertion is made with the arm in abduction. The axillary needles form a pyramidal pattern, which is really the shape of the axilla. A dose of 35 millicuries destroyed can be given safely in the axilla by this method. This irradiation is supplemented by the introduction of radium needles in the infraclavicular region after the plan of Keynes. The needles are plunged directly backward to pierce the pectoral muscles and impinge on the points of the needles introduced directly through the axilla.

Additional needles are placed deeply in the paramammary region, where the principle of a circumferential barrage is employed. One needle extends diagonally across the junction of breast and epigastrium and another lies along the lowermost border of the pectoral fold. Two single cell needles are inserted in the supraclavicular space parallel to the middle third of the clavicle. A Treves needle containing one radium cell is inserted into each of the upper three intercostal spaces in an attempt to block the lymphatic vessels which enter the mediastinum in this location. These needles are placed very close to the sternal margin in order to avoid injury to the internal mammary artery. The dose is never greater than 2 millicuries destroyed for each radium cell. The attached threads for the withdrawal of the needles are tied snugly across the breast and thereby maintain the position of the implants. The arm is kept in abduction while the needles are in place, as this position prevents undue irradiation of the brachial plexus and consequent neuritis. A diagram for the record is made of the arrangement of the radium and the location and dose delivered by each needle. The duration of the interstitial irradiation is from five to seven days, although it may vary more or less. Extraction of the needles can usually be accomplished without anesthesia.

The pursuance of this plan of treatment will meet with some success. It is so conceived that it should destroy any mammary cancer so treated, were it not for unavoidable technical errors. The dose delivered is epidermicidal, and the vesication and injury to the skin are responsible for a long convalescence and considerable distress.

THE HYDRODYNAMICS OF THE RELIEF OF DISTENTION IN THE GASTRO-INTESTINAL TRACT BY SUCTION APPLIED TO INLYING CATHETERS

JOHN RANDOLPH PAINE, M.D.
MINNEAPOLIS

INTRODUCTION

The clinical use of nasal catheter suction-siphonage on over two thousand patients presenting a great variety of pathologic conditions at the University Hospitals during the past four years has amply proved how distention and stasis in the stomach and small intestine may be satisfactorily controlled.[1] The technic of its application and the indications and contraindications for its use as well as the results which may be achieved have been reported.[2]

In the following thesis an attempt is made to elucidate some of the mechanicophysiologic principles concerned and the manner in which distention is prevented or preexisting distention is relieved by the use of this method.

Historical Background.[3]—The use of tubes inserted through the esophagus to relieve gaseous distention probably dates from 1767; when Alexander Monro II, of Edinburgh, employed a flexible tube of coiled wire covered with leather to remove fermenting fluids and gases from the stomachs of cattle.[4] Exactly a hundred years passed before this method of treatment was applied to human beings. Adolf Kussmaul [5] in 1867 made a diagnosis of gastric dilatation due to pyloric ulcer in the case of Marie Weiner. She was successfully treated by frequent empty-

From the Department of Surgery, University of Minnesota.

Submitted to the Faculty of the Graduate School of the University of Minnesota in partial fulfilment of the requirements of the degree of Master of Science in Surgery.

1. Paine, J. R.; Carlson, H. A., and Wangensteen, O. H.: Post-Operative Control of Distention, Nausea, and Vomiting: Clinical Study with Reference to Employment of Narcotics, Cathartics, and Nasal Catheter Suction-Siphonage, J. A. M. A. **100**:1910-1917 (June 17) 1933.

2. Wangensteen, O. H., and Paine, J. R.: Nasal Catheter Suction Siphonage: Its Uses and Technic of Its Employment, Minnesota Med. **16**:96-100, 1933.

3. Paine, J. R.: History of Invention and Development of Stomach and Duodenal Tubes, Ann. Int. Med. **8**:752-763, 1934.

4. Monro, A.: De dysphagia, Edinburgh, A. Neill & Socii, 1797, p. 83.

5. Kussmaul, A.: Ueber die Behandlung der Magenereweiterung durch eine neue Methode mittelst der Magenpumpe, Deutsches Arch. f. klin. Med. **6**:455, 1869.

ing and lavage of her stomach by means of a large stomach tube. From this time on gastric lavage was generally accepted as an important adjunct in surgical treatment.

When Gross [6] and Einhorn [7] independently invented the duodenal tube in 1909, the way was opened for the further application of the principle embodied in gastric lavage. Westermann [8] in 1910 and Kappis [9] in 1911 reported small series of cases of severe peritonitis associated with gastro-intestinal stasis in which continuous siphonage drainage of the stomach was done by means of a small tube passed through the nose. Kanavel [10] in 1916, while recommending this method of treatment, suggested that closed systems be used with such tubes. The general use of siphonage drainage of the stomach in postoperative treatment and in any condition accompanied by gastric and intestinal paresis was earnestly advocated by Matas [11] in 1924.

The application of continuous suction to duodenal tubes originated with Ward,[12] of San Francisco, in 1925. In 1929 he described his suction method of treatment for acute general peritonitis, and in 1930 he described the application of the same method for the treatment of acute dilatation of the stomach.[13] In 1931 Wangensteen [14] reported the use of suction applied to inlying duodenal tubes to relieve the distention accompanying certain types of intestinal obstruction and found that in many such cases operative intervention was not needed. Wangensteen and I [15] in 1933 showed that duodenal tubes draining the upper part

6. Gross, M.: A Duodenal Tube: Preliminary Communication, New York M. J. **91**:77, 1910.

7. Einhorn, M.: A Practical Method of Obtaining the Duodenal Contents in Man, M. Rec. **77**:98-101, 1910.

8. Westermann, C. W. J.: Ueber die Anwendung des Dauermagenheber bei der Nachbehandlung schwerer Peritonitisfälle, Zentralbl. f. Chir. **37**:356, 1910.

9. Kappis, M.: Einige praktische Winke zur Behandlung des peritonitischen Ileus, München. med. Wchnschr. **58**:15-17, 1911.

10. Kanavel, A. B.: Continual Stomach Lavage and Continuous Hypodermoclysis in Peritonitis, Persistent Vomiting with Dehydration, and Dilated Stomach, with a Description of a Modified Stomach Tube, Surg., Gynec. & Obst. **33**:483-485, 1916.

11. Matas, R.: The Continued Intravenous "Drip," Ann. Surg. **96**:643, 1924.

12. Ward, R.: Apparatus for Continuous Gastric or Duodenal Lavage, J. A. M. A. **84**:1114 (April 11) 1925.

13. Ward, R.: Acute General Peritonitis, California & West. Med. **31**:395-398, 1929; Acute Dilatation of Stomach, Am. J. Surg. **8**:1194-1195, 1930.

14. Wangensteen, O. H.: The Early Diagnosis of Acute Intestinal Obstruction with Comments on Pathology and Treatment—with a Report of Successful Decompression of Three Cases of Mechanical Bowel Obstruction by Nasal Catheter Suction Siphonage, West. J. Surg. **40**:1-17, 1932.

15. Paine, J. R., and Wangensteen, O. H.: Necessity for Constant Suction to Inlying Nasal Tubes for Effectual Decompression or Drainage of Upper Gastro-Intestinal Tract, Surg., Gynec. & Obst. **57**:601-611, 1933.

of the gastro-intestinal tract were much less efficient when allowed to act as siphons than when constant suction was maintained.

Method Employed.—It is proposed to discuss in this paper the mechanics and physiology of decompression of the distended gastro-intestinal tract with nasal catheter suction-siphonage. Such a discussion entails an explanation of certain physical phenomena occurring in rigid tubes as well as a study of the details and possibilities of the suction apparatus previously described by Wangensteen and me.[2] The pressure changes occurring in the distended small intestine when a negative pressure is created at one end of it have been studied in nine dogs anesthetized with pentobarbital sodium. The effect of air traps on the resultant pressures and the formation of pressure gradients will be explained. Observations were made on the physiologic mechanism of decompression of the distended small intestine with nasal catheter suction-siphonage in seven cats. The question of the optimal negative pressure to be used is discussed. The factors which militate against decompression are mentioned. A physiologic theory to explain decompression by suction is proposed. A short account concerning the decompression of the colon by suction applied to inlying rectal tubes is appended.

MECHANICS OF RIGID TUBES

The small intestine is a distensible flexible tube easily collapsed when a negative pressure is created within its lumen. As it lies in the abdominal cavity the tubes become broken up into a series of loops which lie in all three planes of space. In order to study the transmission of positive and negative pressures through such a system, experiments were made with a system of glass tubes, connected and bent into a series of vertical loops. Other experiments were made on a series of connected glass loops occupying all three planes of space. These were but crude models of the intestine but had the advantage of eliminating the factors of distensibility and collapsibility of the wall, which complicate any experiment with the intestine itself. They served well enough to illustrate certain hydrodynamic principles.

Transmission of Pressure Through Connected Vertical Rigid Loops Partially Filled with Fluid.—It is a hydrodynamic principle that a rigid tube filled with a homogeneous medium transmits an increase or decrease of either a positive or a negative pressure without loss in the process of transmission. If the tube is filled partly with fluid and partly with gas, such is not the case.

A system of connected vertical glass loops was taken, and each loop was half filled with water, as is represented in figure 1. A negative pressure equivalent to 12 cm. of mercury was applied at point *B* with point *A* closed. The pressure at *A* was then measured and found to be only —3.7 cm. of mercury. This loss of pressure in its transmission through the system was supposedly represented by

the difference in the heights of the columns of water in the adjacent loops. The difference in the heights of these columns of water was measured, and their sum was found to be 109 cm. of water. One hundred and nine divided by 13.6 (specific gravity of mercury) gives 8.01, the number of centimeters of mercury. Thus the experimental results checked with the theoretical result within the error of measurement (8.30 cm. of mercury compared to 8.01 cm. of mercury).

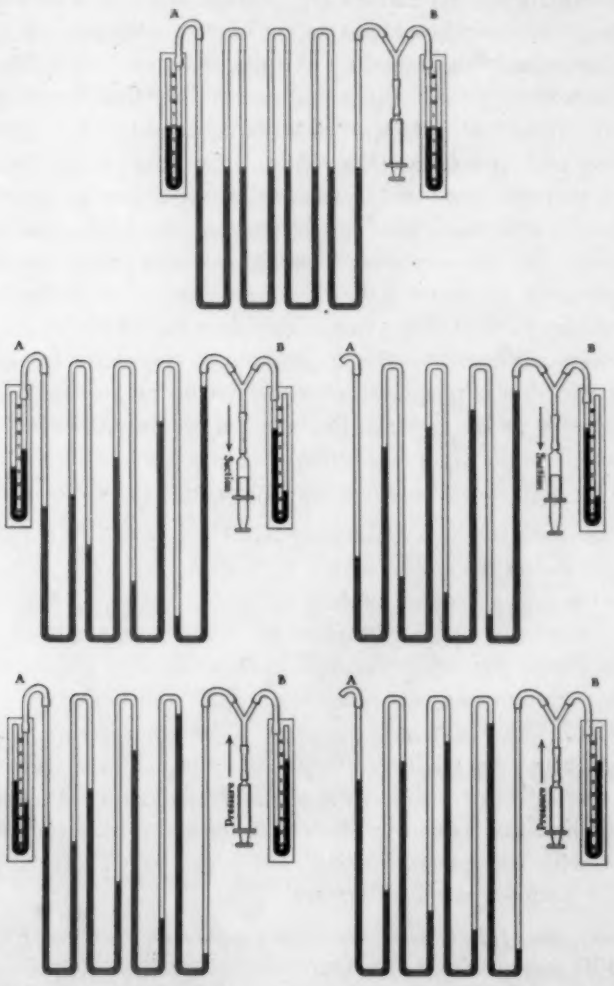

Fig. 1.—Loss in hydrostatic pressure when transmitted through a series of connected vertical rigid loops partially filled with fluid.

The same system of tubes was used again, but instead of applying suction at point *B*, a positive pressure equal to 13 cm. of mercury was used. The pressure at point *A* was found to be 4.4 cm. of mercury. This loss of pressure had again occurred as a result of the formation of unequal columns of water. When the foregoing experiments were repeated with point *A* open, different but analogous results were obtained. The pressure at point *A* in these experiments was the same

as that of the atmosphere, but the formation of unequal columns of water occurred as in the preceding experiments (fig. 1).

When the tubes were completely filled with water, air or an intimate admixture of fluid and gas, such as whipped cream, no loss of either positive or negative pressure occurred in transmission through the system. When whipped cream was used, however, it was observed that after a short time small quantities of liquid cream separated out and collected at the bottom of the loops. Under these circumstances small losses of both positive and negative pressure occurred in transmission through the system.

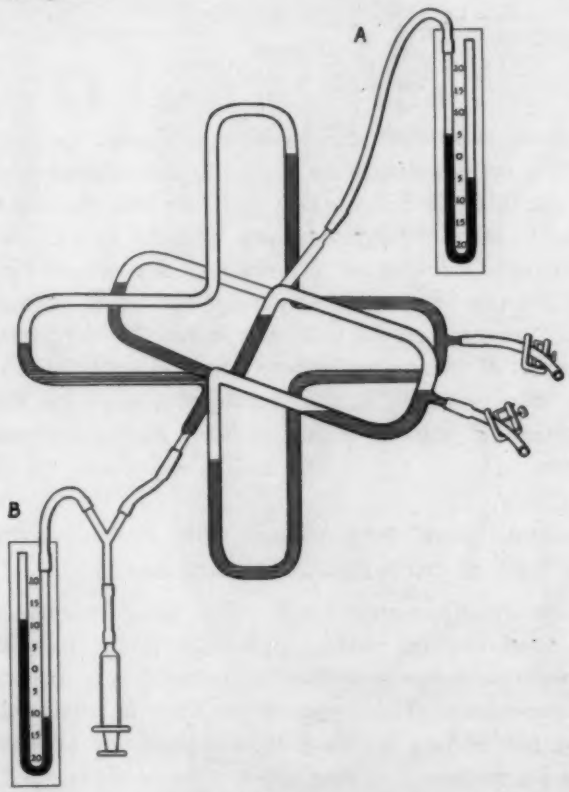

Fig. 2.—Difference in hydrostatic pressure at the two ends of a series of connected rigid loops occupying all three planes of space and partially filled with fluid.

If the tubes were filled as shown in figure 1 and then placed in a horizontal plane, the pressure at points *A* and *B* immediately became equalized, despite any unequal columns of fluid which might have been present before.

Pressure Phenomena in a Rigid Tube with Connected Loops in All Three Planes of Space.—The glass tube represented in figure 2 yielded some interesting observations. A certain amount of water was placed in the system so that about equal parts of water and air were present in each loop. Water manometers were then attached to each end, and the changes in pressure which occurred with movements of the whole apparatus were recorded. Needless to say, the relative position

of the water and the proportions of air and water in any one loop varied with the changes in position of the apparatus as a whole. The recorded pressures were as follows:

Position	A Cm. of Water	B Cm. of Water
1	—11.75	+ 3.0
2	— 8.25	+ 4.5
3	— 9.25	+ 4.5
4	—11.50	+ 6.0
5	— 7.75	+11.0
6	— 5.25	+11.0

These figures show that it is possible to change the pressure at the ends of such a system simply by changing the relative position of the contents of the tube. It follows as a corollary that the changes in pressure are due to the varying quantities of fluid in vertical loops. By various successive changes of position of the whole apparatus, the pressures at the two ends could be finally equalized. It was noted that whenever this occurred all the fluid was in loops which were horizontal. The significance of these observations and the application of the principles which they represent in the decompression of the upper part of the gastro-intestinal tract by nasal catheter suction-siphonage will be discussed later.

MECHANICS AND PHYSICS OF THE NASAL CATHETER SUCTION-SIPHONAGE APPARATUS

Description of Apparatus Used.—The basic mechanical principle involved in nasal catheter suction-siphonage is the maintenance of a continuing negative pressure within a duodenal tube inserted into the stomach or duodenum. This negative pressure is produced and maintained by the use of two bottles with a capacity of approximately 4.5 liters each and a system of rubber tubes. One bottle is filled with water and fitted with a two-holed rubber stopper which contains two glass tubes. One of these glass tubes is short and extends just through the rubber stopper. The other is longer and extends almost to the bottom of the bottle. A length of rubber tubing about 5 feet (152 cm.) long leads from the short glass tube to the second bottle. Another length leads from the longer glass tube and is attached to the duodenal tube. The bottle filled with water is hung inverted from a standard, and enough water is placed in the other bottle just to cover the end of the rubber tubing attached to the shorter glass tube. A diagram of this apparatus is given in figure 3. It is readily seen that this apparatus comprises a modified form of siphon, the head of water held in the inverted bottle serving to make the siphonage action constant when

gas is aspirated through the duodenal tube. A negative pressure is created at the top of the inverted bottle because water tries to run out through the rubber tubing leading to the lower bottle. This negative pressure is transmitted through the longer glass tube and is sufficient to aspirate any gas or fluid in the vicinity of the end of the duodenal

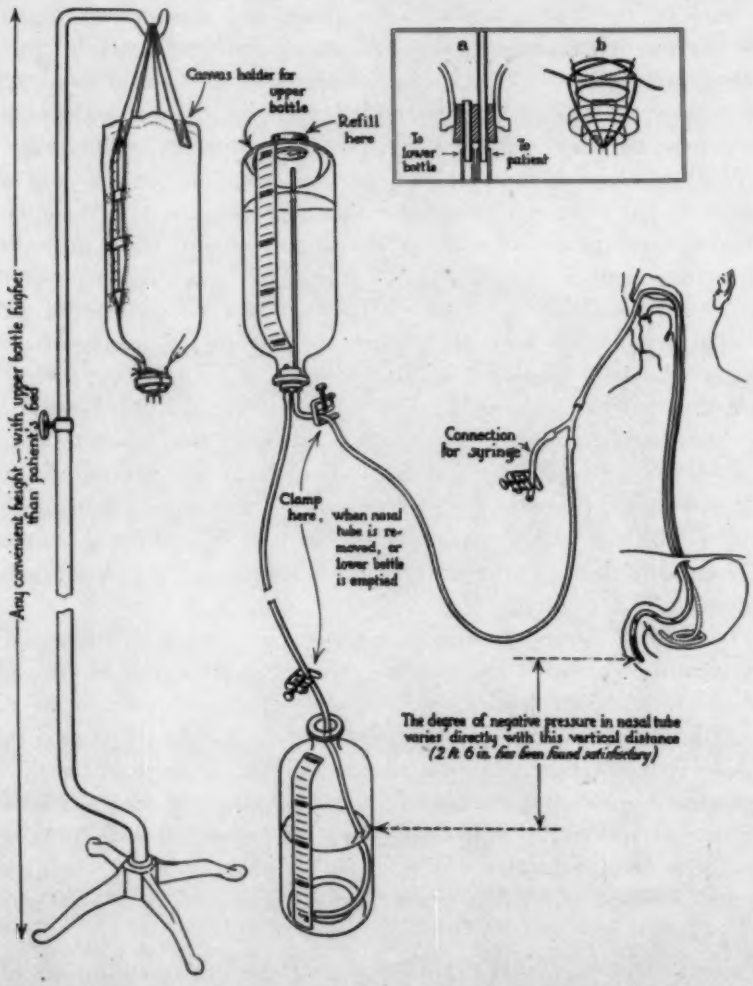
Any convenient height — with upper bottle higher than patient's feet
Canvas holder for upper bottle
Refill here
a
b
To lower bottle
To patient
Connection for syringe
Clamp here, when nasal tube is removed, or lower bottle is emptied
The degree of negative pressure in nasal tube varies directly with this vertical distance (2 ft. 6 in. has been found satisfactory)

Fig. 3.—Diagram of the nasal catheter suction-siphonage apparatus used at the University Hospitals.

tube. This suction action occurs whether the free end of the longer glass tube is below or above the water level in the inverted upper bottle and whether or not fluid or gas is aspirated. If the longer glass tube does not project above the water level in the inverted bottle, however, the effective negative pressure transmitted to the duodenal tube will

be decreased by as many centimeters of water pressure as the end of the tube is below the water level.

If it be assumed that fluid alone is being aspirated, the exact mechanism by which suction occurs can be more easily seen. Under these circumstances two columns of water of unequal height are formed, the taller extending from the level of the water in the inverted bottle to the level of the water in the lower bottle and the shorter extending from the tip of the longer glass tube in the inverted bottle to the perforations in the distal tip of the duodenal tube. Since these columns of water are unequal in height and therefore produce unequal pressures, the shorter column is aspirated into the inverted bottle by the taller one.

While a negative pressure will be maintained as long as any water remains in the top bottle, the degree of negative pressure is dependent on various factors and is constantly changing within fairly wide limits. In practice, both fluid and gas in varying amounts are recovered by the apparatus. The degree of negative pressure transmitted to the duodenal tube varies directly with the proportion of gas present in that tube, the longer glass tube and the rubber tubing connecting them. Gas has little weight and allows the full effect of the column of water running from one bottle to the other to be exerted. As aspiration proceeds, the levels of water in the two bottles gradually shift since the lower bottle fills and the upper bottle empties. When this occurs the column of water which creates the negative pressure in the system is shortened, and consequently the suction exerted through the duodenal tube is decreased.

The actual degree of negative pressure created and the variations in it which occur with the changing conditions mentioned previously were measured in the laboratory by attaching a manometer to the distal end of the duodenal tube by means of a glass Y tube. Figure 4 is the graphic representation of these measurements. It will be noted that the greatest negative pressure which the apparatus will create is between —150 and —160 cm. of water and that this pressure results only when gas alone is being aspirated. When fluid is being aspirated, the greatest negative pressure which can result is between —65 and —70 cm. of water.

Possible Modifications of the Apparatus.—Several modifications of the apparatus are possible. Should a milder degree of suction be desired, the lower bottle which rests on the floor has merely to be elevated and placed on a stool or box. The height of the taller column of water is thereby shortened, and the effective negative pressure furnished by the apparatus is decreased by as many centimeters of water as the lower bottle is raised. On the other hand, increasing or decreasing the height at which the upper bottle is suspended will have no effect on the degree

of negative pressure furnished if fluid alone is being aspirated. However, if gas alone is being aspirated, the degree of negative pressure furnished will be increased or decreased by as many centimeters of water as the upper bottle is raised or lowered. When mixtures of gas and fluid are aspirated, the negative pressure varies between the limits set above, depending on the proportion of gas and fluid passing through the duodenal tube at any one time.

If the distance between the end of the duodenal tube and the level of the water in the lower bottle is increased by placing the patient's bed on blocks, the negative pressure furnished will be increased by as many centimeters of water as the bed is elevated. The greatest negative

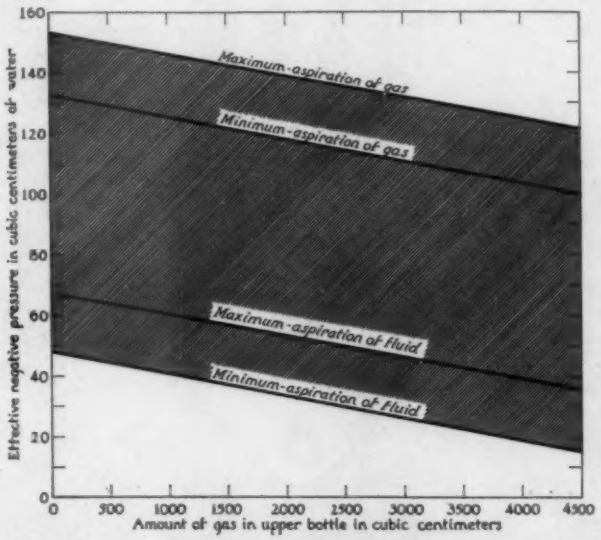

Fig. 4.—The effectual negative pressure created in the duodenal tube by the nasal catheter suction-siphonage apparatus. The variations in this pressure which occur are indicated. At any given time the effectual negative pressure will fall somewhere within the shaded area.

pressure that it is theoretically possible to create with such a system is about —1,000 cm. of water. This limit in the degree of negative pressure is set by the atmospheric pressure. Should a greater negative pressure be required than can be conveniently provided by placing the patient's bed on blocks, two, three or more suction sets may be connected in series, as shown in figure 5. For experimental purposes my associates and I have employed such an arrangement on occasions but have found no benefit to accrue from its use. The duodenal tube itself will collapse with the negative pressure created by such a system, and there is a theoretical danger of necrosis of the mucosa of the stomach or bowel when exceptionally high negative pressures are used.

If a third bottle, as shown in figure 6, is interpolated between the duodenal tube and the inverted bottle, the negative pressure furnished by the apparatus becomes much less variable, and if this bottle is placed on a level with the distal end of the duodenal tube the variations in the negative pressure due to alternate aspiration of fluid and gas or a mixture of both will be practically entirely eliminated. We have frequently used this third bottle to catch aspirated fluid so that it could be returned

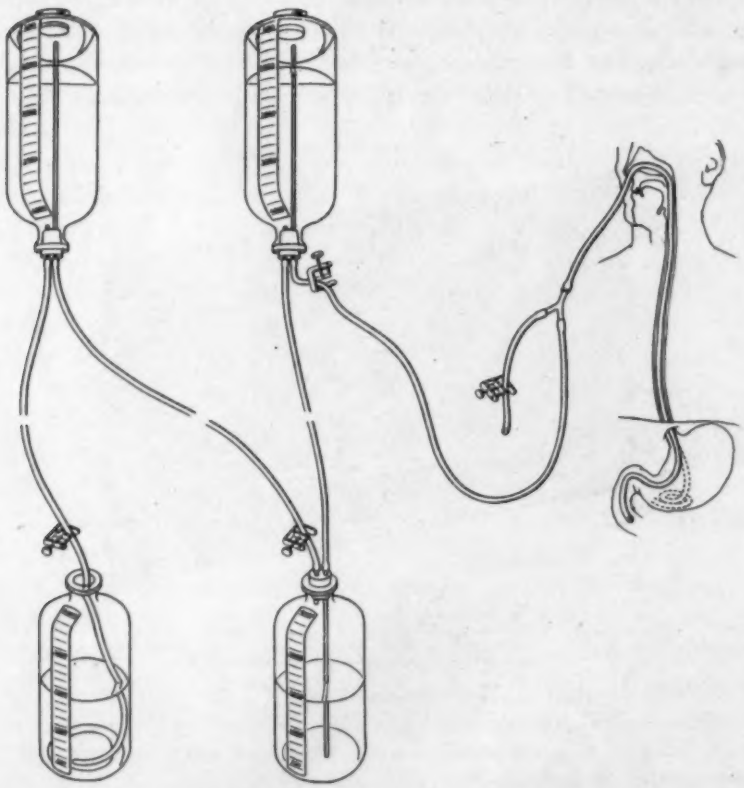

Fig. 5.—The arrangement by which the effectual negative pressure furnished by the nasal catheter suction-siphonage apparatus may be increased to any desired degree up to approximately 1,000 cm. of water.

to the patient in rectal irrigations to make up partially for the loss of fluid which occurs when nasal catheter suction-siphonage is used. This is always done in cases in which large fluid aspirations occur.

Measurement of Aspirated Fluid and Gas.—The amounts of fluid and gas aspirated by the suction apparatus can be easily calculated by simple arithmetic. The gas is collected in the inverted bottle, and its amount can be read directly from a calibrated scale attached to the bottle. Since no two substances can occupy the same space at the same time,

any fluid or gas which passes into the upper bottle must displace an equal volume of fluid in that bottle. The volume of the fluid in the lower bottle, therefore, must be equal to the sum of the volume of fluid which was in it at the beginning and the volume of the fluid and gas aspirated. Two of the three quantities being known, the volume of aspirated fluid is obtained by subtraction.

The amount of aspirated gas which is measured by the scale on the upper bottle is obviously not the true volume. After being aspirated

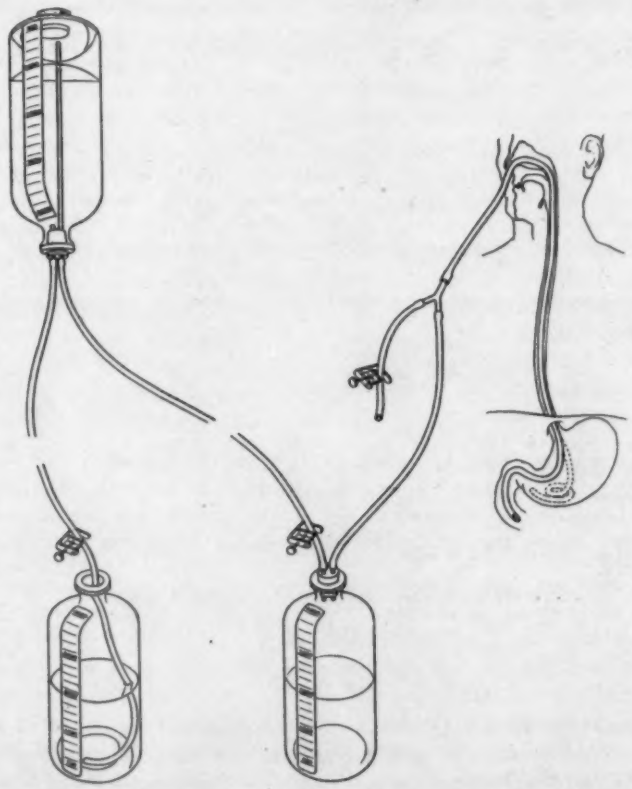

Fig. 6.—The arrangement by which the variations in the effectual negative pressure furnished by the nasal catheter suction-siphonage apparatus may be decreased and by which the aspirated fluid may be caught and returned to the patient as rectal injections if desired.

from the body, the gas decreases in volume owing to the change in temperature which occurs. The gas as it is contained in the upper bottle, however, is constantly at a greater negative pressure than it could possibly be within the gastro-intestinal tract.

If it is assumed that the patient's temperature is 98.6 F., that the pressure of the gas in the intestine is +12 cm. of water pressure and that the gas as contained in the suction apparatus is under —150 cm.

of water negative pressure, it can be calculated that 1,000 cc. of gas as read on the calibrated scale of the suction bottle represents only 892 cc. of gas removed from the patient. Thus the readings are in error by approximately 10 per cent. It is unlikely, however, that this error would ever be of great importance. The difference between the actual volume and the measured volume is relatively insignificant for all clinical purposes.[16]

16. The following is the method by which the amounts of gas and fluid aspirated by the apparatus are calculated.

Readings of fluid levels by the attached calibrated scales when aspiration is begun:

Upper bottle	0 cc.
Lower bottle	400 cc.

Readings of fluid levels after a given period of aspiration:

Upper bottle	1,400 cc.
Lower bottle	2,300 cc.

Gas aspirated is measured directly by reading the fluid level of the upper bottle, i. e., 1,400 cc.

Fluid aspirated is obtained by subtracting 1,400 and 400 cc. from 2,300 cc., i. e., 500 cc.

1,400 cc.	2,300 cc.
+ 400 cc.	— 1,800 cc.
1,800 cc.	500 cc.

Wangensteen has found by actual measurement at operation that the pressure of gas in the distended small bowel of patients with intestinal obstruction varies from + 8 to + 24 cm. of water. Plus 12 cm. is the average pressure found. Slight variations in the intra-intestinal pressure affect the calculated results insignificantly.

Formula to calculate corrected volume of aspirated gas:

$$\frac{VP}{T} = \frac{V'P'}{T'}$$

V indicates the volume of gas in cubic centimeters as measured in suction apparatus; P, the pressure of gas in centimeters of water as contained in suction apparatus; T, the temperature of gas in degrees centigrade calculated from absolute zero as contained in suction apparatus; V', the corrected volume of gas in cubic centimeters; P', the pressure of gas in centimeters of water as present in patient, and T', the temperature of gas in degrees centigrade calculated from absolute zero as present in the patient.

In the example given above the calculation is as follows:

$$\frac{1{,}000 \times 883.6}{294} = \frac{V' \times 1{,}045.6}{310}$$

$$\frac{883{,}600}{294} = \frac{1{,}045.6\ V'}{310}$$

$$3{,}005.44 = 3{,}37\ V'$$

$$V' = 891.8$$

CHANGES IN PRESSURE IN THE SMALL INTESTINE WHEN A NEGATIVE PRESSURE IS CREATED AT ONE END OF IT

The experiments with rigid tubes forming a connected series of vertical loops had shown that an important factor which militated against the evacuation of such tubes with suction when they were partly filled with fluid was the rapid decrease in the force of suction due to the formation of unequal columns of fluid. Similar experiments were performed on the small intestine itself.

Experiment on Human Small Intestine Removed at Autopsy.—A complete small intestine was removed from a body at autopsy and arranged in a large pan to simulate as closely as possible the kinks and loops present in the living abdomen. The distal end was tied with tape around a glass tube which was connected to a water manometer. A duodenal tube was inserted into the proximal end for a short distance, and the intestine was tied around this with tape. Water and air were injected alternately through the duodenal tube in quantities of 50 cc., while the pressure developed in the distal portion of the intestine was noted on the manometer. Two thousand, two hundred and fifty cubic centimeters of water and an equal quantity of air were injected when the manometer recorded a pressure of + 21 cm. of water. The intestine was markedly distended and tense. Although the pressure at the proximal end was not measured, it was thought to be considerably higher than at the distal end, judging from the tenseness of the wall of the bowel. Further quantities of gas and water were then injected until a pressure of 33 cm. was finally built up in the distal portion of the intestine. The contained gas and water were then allowed to escape of their own accord through the duodenal tube. The pressure at the distal end as recorded by the manometer, however, fell to only + 27 cm. of water. With the application of suction to the duodenal tube an additional large amount of gas and fluid was removed from the intestine, and the 8 inches (20.3 cm.) of the duodenum adjacent to the duodenal tube became entirely collapsed. The pressure recorded by the manometer fell to + 18 cm. of water.

Experiments on Small Intestines of Anesthetized Dogs.—The same experiment in a slightly more elaborate form was next carried out on nine dogs previously starved for twenty-four hours and anesthetized with pentobarbital sodium given intravenously. In these dogs the abdomen was first opened, and a tight tape ligature was placed around the terminal portion of the ileum. Just above this ligature a glass tube connected to a water manometer was placed in the bowel. A duodenal tube was then inserted into the duodenum, and the bowel was tied closely around it with tape. Varying quantities of air were injected through the duodenal tube in five of the dogs and air and water in four. The hydrostatic pressure which the manometer recorded was noted, and then suction was applied to the duodenal tube. The same degree of negative pressure that is used clinically was employed. The change in the manometer reading gave the effect of the suction as transmitted through the length of the bowel. The segment of intestine immediately adjacent to the tip of the duodenal tube immediately became collapsed and entirely empty of both fluid and gas soon after the application of suction. Table 1 presents the results of these experiments in tabulated form. It is to be noted that in only one instance did the pressure in the terminal ileum become zero, and in that instance the intestine had been distended with air alone. This is significant.

Air Traps and Pressure Gradients.—From table 1 it is seen that the average decrease in pressure in the terminal portion of the ileum

was slightly better when gas alone was used to distend the bowel than when both gas and water were used. This difference appeared to be due to the division of the water contained in the bowel into unconnected portions and the consequent formation of air traps. The inability to reduce the ileal pressure consistently to zero when gas alone was employed to distend the bowel appeared to be due to the kinking of the bowel at irregular intervals as it lay in the abdominal cavity.

Additional evidence that kinks and air traps in the bowel prevent the free transmission of hydrostatic pressure along the length of the

TABLE 1.—*Immediate Pressure Changes in the Terminal Portion of the Ileum of Dogs After the Application of from 70 to 150 Cm. of Water Negative Pressure to a Duodenal Tube in the Duodenum* *

Dog	Amount of Water and Air Used to Distend Small Intestine, Cc.		Amount of Water and Air Removed from Distended Small Intestine by Suction, Cc.		Pressure in Terminal Portion of Ileum, Cm.		Percentage Decrease in Pressure of Terminal Ileum Due to Suction
	Air	Water	Air	Water	Before Application of Suction, Water	After Application of Suction, Water	
1	120	...	...†	...	8.0	2.5	69.0
2	100	...	70	...	9.6	0.0	100.0
3	250	...	150	...	26.5	10.0	62.0
4	300	...	225	...	28.0	5.0	82.0
5 a	560	...	235	...	76.2	35.4	53.0
b	535	...	375	...	81.6	29.9	63.0
Average					38.3	13.8	71.5
6	300	800	60	125	19.0	14.0	26.0
7	...†	...†	...†	...†	38.0	14.0	63.0
8	75	500	0	225	56.0	15.0	73.0
9	450	200	...†	...†	70.0	5.0	93.0
Average					45.8	12.0	64.0

* All dogs were previously starved for twenty-four hours. For all practical purposes the small intestine was empty.

† Quantities not measured.

intestine was found in experiments of a similar nature in which the intra-enteric pressure was measured by manometers at different places along the bowel. If quantities of air, water or both are injected at one end of the small intestine, a gradient of pressure will be found, the pressure tending to decrease as the point of measurement becomes further removed from the source of the injection. The reverse of this is also true. Given a bowel distended with air, water or both and apply suction at one end. Measurements of pressure at intervals along the bowel starting near the point of suction will show an increasing gradient of pressure. These facts were found to be true by experiments on six dogs anesthetized with pentobarbital sodium injected intravenously. These dogs were all starved for twenty-four hours before the experiments so that their small intestines were empty and collapsed. A lapa-

rotomy was performed, and the terminal portion of the ileum was occluded with a tape tie. A duodenal tube was then passed through the stomach and into the duodenum. The duodenum was tied around the tube by means of tape. Air and water were injected into the intestine either through the duodenal tube or by means of fine needles inserted obliquely through the wall of the bowel. A negative pressure of from 70 to 150 cm. of water was created in the duodenal tube when desired

TABLE 2.—*Pressure Gradients in the Distended Small Intestine of Dogs*

Dog		Pressure in Cm. of Water		
		Duodenum	Jejunum	Ileum
10	80 cc. of air injected into ileum	14.6	12.5	24.8
	Three hours later	2.0	7.0	0.5
	30 cc. of air injected into duodenum	9.0	7.5	8.0
	Suction applied to duodenal tube	2.0	3.0	2.5
11	100 cc. of air injected into duodenum	27.2	0.0	0.0
	Eight minutes later	26.0	8.1	16.3
	Eleven minutes later	25.0	10.0	15.0
	200 cc. of air injected into duodenum	32.6	8.1	19.0
	100 cc. of air injected into duodenum	32.6	27.2	21.8
	200 cc. of air injected into duodenum	32.6	35.4	38.1
	200 cc. of air injected into duodenum	54.4	43.5	43.5
	Air allowed to escape through duodenal tube	0.0	13.6	21.8
12	100 cc. of air injected into duodenum and 50 cc. of air injected into jejunum			
	Thirty minutes later	38.0	27.0	38.0
	50 cc. of air injected into duodenum	81.6	43.5	46.2
	200 cc. of air injected into duodenum	84.3	76.1	81.6
	Suction applied to duodenal tube (375 cc. of air aspirated)	16.3	19.0	29.9
	400 cc. of air injected into duodenum	76.2	68.0	76.2
	Suction applied to duodenal tube (350 cc. of air aspirated)	16.6	20.4	35.4
13	50 cc. of air injected into ileum	7.0	10.6	10.4
	Fifteen minutes later	0.6	4.6	0.8
	50 cc. of air injected into ileum (15 minutes later)	4.0	7.0	9.6
	Suction applied to duodenal tube	0.0	2.6	0.0
14	800 cc. of water and 300 cc. of air injected alternately in small quantities into duodenum	12.0	11.2	0.6
	Suction applied to duodenal tube (125 cc. of water and 60 cc. of air aspirated)	6.2	7.4	0.4
15	50 cc. quantities of air and water injected alternately into duodenum until	38.0	....	30.0
	Suction applied to duodenal tube	0.0	0.0	14.0

by connecting it to a suction apparatus. Intra-intestinal pressures were measured by inserting a needle connected to a water manometer obliquely through the wall of the bowel. One of these experiments is reported in detail. A summary of the results obtained on the six dogs appears in table 2.

Experiment on the Distended Small Intestine of a Dog, Showing Formation of Pressure Gradients.—A mongrel dog weighing 17 Kg. and previously starved for twenty-four hours was anesthetized with 35 mg. of pentobarbital sodium per kilogram injected intravenously. Laparotomy was performed, and the bowel was

arranged to hang over the side of the animal, as shown in figure 7. The bowel measured 140 cm. in length. The terminal ileum was tied with tape. A duodenal tube was inserted through the stomach into the upper part of the jejunum and held in place with a tape tied around the bowel. Air and water were injected alternately in quantities of 50 cc. through the duodenal tube. Pressures were measured by puncturing the bowel obliquely with a small needle attached to a water manometer. A pressure of 30 cm. of water was finally built up in the distal end of the intestine. The pressure in the proximal portion was 38 cm. of water. From 70 to 150 cm. of negative pressure was applied to the duodenal tube. The pressure in the distal portion of the intestine fell to 14 cm. of water and remained constant. The proximal 10 cm. of the intestine became completely collapsed. Pressures were then measured along the course of the intestine as shown in figure 7.

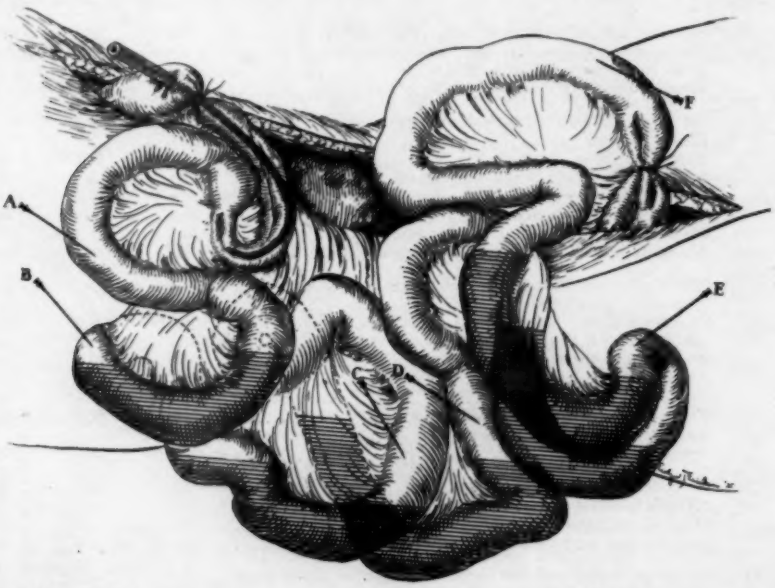

Fig. 7.—Typical pressure gradient occurring in the distended small intestine of the dog. The intestine has been filled partly with water and partly with air. The pressures at *A* and *F* before the application of suction to the duodenal tube were plus 38 cm. of water and plus 30 cm. of water, respectively. After the application of suction to the duodenal tube pressures in centimeters of water were recorded as follows: *A*, 8 cm.; *B*, 10 cm.; *C*, 10 cm.; *D*, 12 cm.; *E*, 15 cm., and *F*, 14 cm.

OBSERVATIONS ON THE PHYSIOLOGIC MECHANISM OF DECOMPRESSION OF THE SMALL INTESTINE OF CATS WITH NASAL CATHETER SUCTION-SIPHONAGE

In order partially to visualize what occurs in the distended human abdomen when suction is applied to a duodenal tube lying in the stomach or duodenum, observations were made on seven cats. In five of these animals a negative pressure equivalent to that used clinically was

employed. In the other two animals a negative pressure about one-half as great as that used clinically was employed.

Technic of the Experiments.—The observations were made as follows: Surgical anesthesia was obtained by the intraperitoneal injection of pentobarbital sodium. A laparotomy was performed, and the small intestine was measured. A duodenal tube was then passed into the stomach or through the stomach into the duodenum. The size of the intestine and any distention due to gas or fluid were noted. Quantities of air varying from 25 to 80 cc. were then injected into the intestine by means of a fine needle and syringe. The point of injection was varied from time to time. The abdomen was then closed, and suction was applied to the duodenal tube. After from one-half to two hours, the amount of gas aspirated was recorded, and the abdomen was reopened. The intestines were reinspected for changes in the disposition of the gas and the degree of decompression which had occurred. Further quantities of gas were then injected as before, and the whole procedure was repeated three or four times.

Observations Made and Discussion of Their Importance.—The experiments are presented in tabulated form in table 3. The observations all tended to show that while suction applied to a duodenal tube in the stomach was highly efficient in decompressing the stomach alone, it was necessary to insert the tube through the pylorus into the duodenum to obtain satisfactory decompression of the small intestine. In other experiments on cats, not reported here, it could be demonstrated that while the pylorus is occasionally patent to the passage of gas, usually a pressure of from 10 to 15 cm. of water in the duodenum was necessary to force any gas into the stomach from the intestine. This presupposes, of course, that the pylorus is in a state of contraction. It is to be appreciated that in the normal animal there is a rhythmic relaxation of the pyloric sphincter, and this intermittent relaxation seems to be the explanation for the not infrequent decompression of the small intestine which has been observed clinically in patients when the tip of the duodenal tube has remained in the stomach. The fact, however, that it was necessary to insert the duodenal tube into the duodenum in order to insure satisfactory decompression of the artificially distended small intestine of the cat is also borne out by clinical experience. Numbers of cases have been seen in which it has required from twelve to thirty-six hours to pass the duodenal tube through the pylorus with little or no decompression occurring during this period. On the other hand, when the duodenal tube at last passed beyond the pylorus a more or less constant aspiration of gas occurred with a concomitant decrease in the distention.[17]

17. Wangensteen, O. H.: Therapeutic Considerations in Management of Acute Intestinal Obstruction: Technic of Enterostomy and Further Account of Decompression by Employment of Suction Siphonage by Nasal Catheter, Arch

(Footnote continued on next page)

The intestine being an elastic tube, distention occurring in one segment tends with the passage of time to be more or less evenly distributed until all portions of the tube partake of it in a like degree. This fact was observed in the experiments on the seven cats. The equalization

TABLE 3.—*Observations on the Physiologic Mechanism of Decompression with Nasal Catheter Suction-Siphonage of the Small Intestine of Cats*

Cat	Length of Intestine, Cm.	Distance Below Pylorus at Which Air Was Injected, Cm.	Total Air Injected, Cc.	Degree of Negative Pressure Used, Cm. of Water	Quantity of Gas Recovered and Time Required with End of Duodenal Tube in: Stomach	Duodenum	Comment
1	30	17	80	150	0 cc. 1.5 hr.	10 cc. 1 hr.	40 cc. of air distended 20 cm. of small intestine; after 1½ hr. the distention was more evenly distributed; 80 cc. of air distended most of the small intestine; after 1 hr. the duodenum was collapsed
2	70	23	100	150	25 cc. 2.5 hr.	5 cc. 2 hr.	100 cc. of air distended the upper two thirds of the small intestine and some air passed into the stomach
3	85	28	125	115	35 cc. 3 hr.	30 cc. 2 hr.	50 cc. of air distended 40 cm. of small intestine; 100 cc. of air distended the whole small intestine and forced some air into stomach and cecum; at the end of 5 hr. most of gas in the bowel had disappeared although only one half of it had been recovered with suction
4	120	45	125	150	....	35 cc. 2 hr.	100 cc. air distended entire small intestine and some air passed into stomach and cecum; after 2 hr. the small intestine was still evenly distended except for 10 cm. of duodenum adjacent to the tip of the duodenal tube
5	120	50	130	150	....	40 cc. 2 hr.	Entire small bowel was distended; when suction was applied 10 cm. of duodenum became collapsed immediately; after 2 hr., 30 cm. of small intestine below the duodenal tube was collapsed; the remainder of the small intestine was evenly distended; peristalsis was fairly active
6	120	75	130	150	....	115 cc. 4 hr.	Peristalsis was quite active; at the end of 4 hr. only a small part of terminal ileum remained distended; increments of gas were seen continually passing up into the collapsed duodenum
7	130	125	100	115	....	65 cc. 1.5 hr.	Peristalsis was active; after 1 hr. the small intestine was much less distended than before; small quantities of gas were constantly being pushed up around the duodenal tube

Surg. **26**:933-961 (June) 1933; The Management of Acute Intestinal Obstruction with Special Mention of the Character of the Vomiting and Distention, Journal-Lancet **54**:640-645, 1934. Wangensteen, O. H., and Paine, J. R.: Treatment of Acute Intestinal Obstruction by Suction with Duodenal Tube, J. A. M. A. **101**:1532-1539 (Nov. 11) 1933.

of pressure was far from perfect, but the tendency was present just the same, and the degree with which it occurred varied with the degree of peristalsis present in the bowel.

In a distended elastic and easily collapsible tube the application of suction to one portion of it immediately and completely evacuates and collapses that portion of the tube which is immediately adjacent to the point of negative pressure. If suction is applied to a distended elastic tube, the walls of which are not easily collapsible, the decompression will be complete throughout its length, provided kinks do not occur which occlude the lumen. The small intestine of both man and animals is both elastic and collapsible. When suction is applied to one portion of it the wall is immediately collapsed down around the point of negative pressure, and in the cat these collapsed portions of intestine measured from 6 to 10 cm. With the collapse of the walls the force of the suction sucked the mucosa tightly into the openings of the tube, holding it there with a force dependent on the degree of negative pressure used. This having occurred, no further decompression took place until with the passage of time gas slowly passed up from the portion of the intestine left distended and filled the collapsed portion. Under these circumstances if the duodenal tube or the adhering wall of intestine were slightly moved either by the movements of the intestine itself or by manipulation, decompression of the segment occurred again.

It is probably true that the foregoing mechanism is really the manner in which nasal catheter suction-siphonage effectually decompresses the distended intestine. In the two cats in which intestinal peristalsis was most active during the period of observation the best decompression was obtained. In these animals the sequence of events outlined occurred repeatedly, peristalsis slowly refilling the collapsed portion of intestine from the gas in the portion still distended. Such a theory of decompression seems to give the best explanation for the rather poor results not infrequently obtained in attempts to decompress an established distention due to paralytic ileus and the more rapid and complete decompression experienced in certain cases of mechanical obstruction in which peristalsis is hyperactive.

Optimal Negative Pressure.—The sucking of the wall of the bowel against the openings of the duodenal tube brings up two important questions. These are: 1. Will necrosis of the wall of the bowel occur at the points where the mucosa tends to be herniated into the openings of the duodenal tube? 2. Will milder degrees of negative pressure be more effective in attempts at decompression?

During the past four years at the University Hospitals necrosis of the wall of the bowel or of the mucosa was not observed at autopsy on thirty experimental animals that had been subjected to nasal catheter

suction-siphonage or on patients who had been treated by this method. Until further experimental work has been done, the second question cannot be satisfactorily answered. The limits of negative pressure with which decompression may be accomplished are probably fairly wide. The degree of suction that the siphon apparatus which we employ furnishes has proved satisfactory in clinical use. Negative pressure two and three times as high as that usually employed was not suitable because it collapsed the rubber tubing as well as the duodenal tube. A negative pressure approximately half that usually used has been tried on a fair number of patients and on eight or ten animals. The results have not been strikingly different from those obtained with stronger suction. One disadvantage of the milder degrees of negative pressure seems to be that mucus and the less fluid portions of the intestinal contents may more easily occlude the relatively small lumen of the duodenal tube. One gets the impression that the usual full strength suction is within the range of optimal values.

FACTORS MILITATING AGAINST DECOMPRESSION OF THE DISTENDED SMALL INTESTINE BY NASAL CATHETER SUCTION-SIPHONAGE

The observations made on the behavior of gas and fluid in rigid tubes have indicated several things which have a direct bearing on the decompression of the distended gastro-intestinal tract. It is well known that the intimate admixture of gas and fluid which is found in the normal intestine is not present in cases of stasis when distention occurs. Instead, the gas and water separate out, although the relative quantity of each present may vary greatly. Segments of the intestine became alternately filled with gas and fluid. The conditions studied in the vertical glass loops are thus reproduced to a certain extent. Suction applied to such an intestine, disregarding for the present the effect of kinks, elasticity and collapsibility of the wall of the bowel, must overcome the factor presented by the columns of fluid present in those loops which happen to be vertical. The presence of fluid in horizontal loops would have no effect except for the kinking and compression of underlying loops which it might cause owing to its weight. It was demonstrated in the measurements made on the glass tube with loops in all three planes how the pressure at different points of the system could be varied practically at will by changing the position of the apparatus as a whole and how the pressure was equalized throughout the system when the apparatus was so turned that all the fluid occupied horizontal loops. If it were possible to visualize perfectly the contained fluid in the intestine as it lies in the abdominal cavity, an approximation of this effect might be achieved by repeatedly turning the body in various direc-

tions. The positions of four dogs and several patients were changed repeatedly but with little or no improvement over results obtained without such maneuvers.

The presence of kinks in the bowel must be an important factor decreasing the efficiency of suction used for the purposes of decompression. Such kinks when formed or maintained by the weight of overlying loops must be real blocks to the equalization of hydrostatic pressure along the lumen of the bowel. This paper contains no experimental work on that point.

The collapsibility of the intestinal wall is a factor which has consistently entered into most of the experimental work discussed. It has always occurred immediately adjacent to the point of suction as soon as the fluid and gas contained in that portion of the bowel have been removed, and it has temporarily at least caused the process of decompression to cease until manipulation, peristalsis or the equalization of pressure due to elasticity partly redistends the collapsed portion. If it were not for the fact that even a mild degree of negative pressure produces this collapse, it might be possible to decompress a distended intestine rapidly by employing a fairly high degree of suction which would immediately overcome the other factors such as vertical columns of water and kinks in the bowel. However, I see no purpose to be served by using a greater negative pressure than suffices to remove gently the accumulations of gas and fluid which occur in the segment of the intestine immediately adjacent to the point of suction. As stated previously, the degree of negative pressure used clinically for decompression at the University Hospitals is probably within the range of optimal values.

PROBABLE PHYSIOLOGIC MECHANISM OF DECOMPRESSION

It will be worth while to try to integrate all the preceding observations and to describe the probable sequence of events which occurs when a distended small intestine is decompressed by suction applied to a duodenal tube. When the tube, perforated at intervals for about 9 inches (23 cm.) proximal to its tip, enters the stomach, this organ will be immediately and almost entirely emptied of both fluid and gas. The tube itself will then lie between the collapsed walls of the stomach. Should the tube be inserted no further along the gastro-intestinal tract, decompression of the bowel may or may not take place, depending principally on the tone of the pyloric sphincter and the strength of intestinal peristalsis. With the duodenal tube in the stomach, any gas it succeeds in removing from the small intestine must be brought to it by regurgitation from the duodenum. Such a tube, however, will be quite efficient in preventing an existing distention of the small intestine from increas-

ing or in preventing such a distention from occurring. Hibbard,[18] as well as McIver,[19] have shown by qualitative and quantitative analyses of intestinal gases that swallowed air is responsible for approximately 70 to 75 per cent of the gas present in the obstructed bowel. As the duodenal tube is gradually inserted further, it will finally pass through the pylorus and enter the duodenum, being propelled chiefly by gastric peristalsis but partly by its weight, if the patient be made to lie on his right side. During this period of transit, small quantities of both fluid and gas may be regurgitated through the pylorus. These will be immediately evacuated when they reach the vicinity of the tube. As soon as the duodenal tube has entered the duodenum decompression of this portion of the intestine proceeds rapidly until the walls of the intestine lie collapsed around the tube and held to it by the force of the suction. Since the perforations in the duodenal tube extend about 9 inches proximal to its tip, suction is maintained simultaneously in both the duodenum and the stomach. This effectively prevents any air swallowed from causing gastric dilatation. Concomitant with the decompression of the duodenum a decrease in the intraluminary pressure of the intestine occurs throughout its entire length. The decrease becomes less as the terminal ileum is approached. Columns of water are set up which, with the kinks in the bowel, tend to equalize the force of the suction. Movements of the patient and the peristalsis of the intestine as well as the elasticity of the wall of the bowel cause increments of both gas and fluid to pass up into the collapsed portion from the still distended more distal portions. These quantities of gas and fluid which finally reach the vicinity of the duodenal tube are evacuated when some movement of the patient or of his intestine momentarily dislodges the adherent wall of the bowel from the perforations in the duodenal tube. In this manner, with the passage of time, the process proceeds slowly until the entire small intestine has been decompressed.

DECOMPRESSION OF THE DISTENDED COLON BY MEANS OF SUCTION APPLIED TO INLYING RECTAL TUBES[20]

Soon after the first clinical use of nasal catheter suction-siphonage it was appreciated that a preexisting distention of the colon was affected

18. Hibbard, J. S.: Gaseous Distention Associated with Mechanical Obstruction of the Intestine, Arch. Surg. **33**:146-167 (July) 1936.

19. McIver, M. A.; Benedict, E. B., and Cline, J. W.: Postoperative Gaseous Distention of the Intestine, Arch. Surg. **13**:588-604 (Oct.) 1926.

20. When colostomy has been performed for purposes of decompression in patients with obstruction of the large bowel the colon is often opened just enough to allow a rectal tube to be inserted into the lumen of the bowel. The application of suction to such tubes has seemed to aid decompression of the distended segment

little or none by its use. Sperling [21] has shown that the ileocecal valve is patent in the vast majority of patients to the retrograde passage of fluid or gas except under much higher pressure than physiologically occurs. This being true, suction applied to a nasal catheter inserted into the stomach or duodenum can affect a distention of the colon only by preventing the passage of swallowed air through the small intestine and into the already distended colon. Therefore, while suction applied to a nasal tube may not decrease a preexisting distention of the large bowel, it is of distinct benefit in decreasing the increase of such a distention.

The use of continuous suction applied to an inlying rectal tube as an aid in the control of colonic distention has been tried by various men with varying results. Pratt,[22] of New York, has been the most enthusiastic of these. In our own experience the procedure has not been very successful. On purely mechanical grounds its use would appear to be limited to cases of paralytic (inhibitive) ileus or obstruction of the colon on a neurogenic (spastic) basis in which no true mechanical obstruction existed.

Difficulties to Be Overcome in Decompression of the Colon.—In whatever type of obstruction of the large bowel it is used, negative pressure applied to an inlying rectal tube must overcome certain inherent difficulties before satisfactory results can be expected. The factors which most strongly militate against successful decompression are: (1) the more or less solid character of the content of the lower part of the bowel and (2) the inability to pass a rectal tube above the sigmoid flexure of the colon. In a previous section of this paper the optimal negative pressure to be used in decompression with suction has been discussed. Such a discussion is particularly pertinent in any consideration of decompression of the colon.

Efforts to Overcome the Difficulties.—It is readily appreciated that the more solid content of the lower part of the bowel requires greater negative pressure to draw it off through a tube than the contents of the small bowel require. In our experience it has been found that even if

---

and lessened the danger of infection which a more complete immediate opening of the colostomy might produce.

The application of suction to enterostomy tubes has been practiced as a routine in cases of obstruction of the small bowel in which duodenal suction has not been entirely successful in decompressing the distended loops. These cases have not been studied critically enough to say whether any advantage accrues from such a procedure, but it has permitted us to measure the amount of gas escaping through the enterostomy tube.

21. Sperling, L.: Rôle of the Ileocecal Sphincter in Cases of Obstruction of the Large Bowel, Arch. Surg. **32**:22-49 (Jan.) 1936.

22. Pratt, G. H.: Intestinal Evacuation by Hydraulic Suction: Further Uses of Suction-Siphonage, Am. J. Surg. **23**:148-156, 1933.

negative pressures of two or even three times that used for the small bowel is employed, feces lodge in the openings of the rectal tube and effectively prohibit all suction. In an effort to obviate this difficulty, periodic irrigations of the colon and the rectal tube have been used, but with no great improvement in the practicability of the method. The use of double recurrent rectal tubes suggested itself as a possible means of securing a sufficient dilution of the feces to enable them to be drawn off. A no. 36 French rectal tube with four or six perforations in the side wall for the efferent tube and a no. 14 French catheter for the afferent tube have been used. These tubes were taped together and inserted in the rectum as far as possible without kinking. Tap water was used for irrigation. Fairly satisfactory results were obtained as far as the feces were concerned, but little or no decompression occurred proximal to the sigmoid flexure.

The rectum and sigmoid flexure of the colon present the most tortuous path found in the gastro-intestinal tract. This fact enhances greatly the difficulty encountered in blindly passing a flexible tube along its lumen and prevents a negative pressure created in the rectum from being at all effectual in the descending colon. We have repeatedly attempted to insert a rectal tube up into the sigmoid flexure, guiding it with the forefinger inserted through the anus along the side of the tube. In only one case has it been possible to insert such a tube more than 5 or 6 inches (12 to 15 cm.) without having it become caught in one of the numerous folds of mucous membrane and kinked to such an extent that suction applied to the distal end exerted no effect whatever. In one case the tube was easily passed well up the descending colon to the neighborhood of the splenic flexure.

Attempts to pass tubes into the descending colon through a sigmoidoscope have also proved unavailing. A height of from 18 to 20 cm. from the anus can uniformly be reached, but we have not yet been able to perfect a technic which will allow the tube to pass the acutely angulated sigmoid flexure.

Experiments Performed on Cadavers.—In four cadavers with the abdomen widely open and the viscera, with the exception of the colon, removed an attempt was made to evolve a technic which would permit a satisfactory decompression of the distended large bowel. In three of these four cadavers the lower part of the bowel contained considerable amounts of feces. The distal half of the colon in the fourth cadaver was practically empty.

Repeated attempts to pass a rectal tube above the sigmoid flexure without intra-abdominal manipulation were all unsuccessful in each of the four cadavers. Invariably the presenting tip of the tube once past the valves of Houston followed up the curve of the sacrum and impinged on the wall of the sigmoid flexure. Attempts to pass it further with the colon collapsed or distended tended to produce a sacculation in the wall of the bowel. It is conceivable that energetic attempts to insert the tube farther might possibly produce a perforation, although this did not occur in any of the cadavers studied. No amount of manipulation of

the tube could make it take the sharp turn to the left necessary to reach the descending colon.

It had been previously suggested that while the passage of a rectal tube above the sigmoid flxure might be impossible in the usual case, such a procedure would be possible at the time of laparotomy when the advantages of intra-abdominal manipulation could be obtained. We found this to be invariably the case in the four cadavers studied.

The colons were distended, and attempts were made to decompress them by connecting a water siphon to an inlying rectal tube. When the rectal tube was below the sigmoid flexure, decompression stopped as soon as the rectum had been emptied, the S-shaped flexure forming an almost perfect valve and preventing transmission of the negative pressure. The feces present in three of the cadavers were also effective in stopping the suction action, but this difficulty could satisfactorily be overcome by repeated injections of water alternated with periods of aspiration. When the colon was enormously distended so that the sharp turns in the bowel at the sigmoid flexure were partially straightened out some decompression of the entire colon could be obtained, but not enough to seem to warrant the use of such procedures on patients.

Granted that the rectal tube could be inserted as far as the descending colon, it remained to see what degree of decompression could then be accomplished. In the cadavers studied we were able to obtain satisfactory decompression of the entire descending colon but only very imperfect decompression of those portions of the colon proximal to the splenic flexure. The repeated injection of water through the rectal tube followed by short periods of suction did not effect any greater degree of decompression.

SUMMARY

Alexander Monro II, of Edinburgh, in 1767 used tubes inserted through the esophagus to remove fluids and gases from the stomachs of cattle. Adolph Kussmaul in 1867 applied this method to human beings with success. The application of continuous suction to inlying duodenal tubes originated with Ward, of San Francisco, in 1925. In 1931 Wangensteen further developed this method of combating intestinal stasis and distention. He used it with marked success in selected cases of acute mechanical obstruction.

Positive and negative pressures transmitted through a system of connected vertical rigid tubes, partially filled with fluid, are decreased in their transmission owing to the formation of unequal columns of water.

If a glass tube partially filled with water is bent to form loops in all three planes of space, the hydrostatic pressure at each end of the tube may be altered by changing the relative position of the system as a whole.

The nasal catheter suction-siphonage apparatus used at the University Hospitals is a water siphon so modified as to produce a continuing negative pressure within an attached duodenal tube. The effectual negative pressure furnished by the apparatus depends on several factors, chief of which are the relative position of the bottles with respect to the distal end of the duodenal tube and the relative proportions of fluid and gas aspirated at any one time.

The suction apparatus may be modified to produce any range of negative pressure up to — 1,000 cm. of water. By the interpolation of a third bottle the variations in negative pressure due to alternate aspirations of fluid and gas may be diminished. The third bottle may also be used to catch the fluid aspirated so that it can be returned to the patient if desired.

The quantities of gas and fluid aspirated can be calculated from readings on calibrated scales attached to the bottles.

The creation of a negative pressure at one end of the distended small intestine of anesthetized dogs and of a distended human small intestine removed at autopsy caused the immediate complete decompression of that portion of the intestine adjacent to the source of negative pressure and caused partial decompression of the remaining portions of the bowel.

The establishment of a negative pressure at one end of the anesthetized dog's small intestine distended partly with air and partly with water produced a series of air traps and a gradient of pressure.

Decompression of the distended small intestine of anesthetized cats by suction applied to a duodenal tube was periodic. Better results were obtained when the tube was in the duodenum than when it was in the stomach. The most important factor favoring decompression appeared to be movements of the intestines, either peristaltic or otherwise.

The factors which militate against decompression of the distended small intestine by suction are: (1) the formation of vertical columns of fluid and air traps, (2) kinks in the bowel and (3) collapsibility of the intestinal wall.

Decompression of the distended colon by means of suction applied to inlying rectal tubes is a great deal less satisfactory than is decompression of the distended small intestine by means of suction applied to inlying duodenal tubes, owing to the more solid nature of the contents of the large bowel and to the tortuous course of the sigmoid flexure of the colon.

CONCLUSIONS

1. Decompression of the distended small intestine by means of suction applied to an inlying duodenal tube is a satisfactory method of relieving distention.

2. The success of this method depends on the maintenance of a continuous moderate degree of negative pressure within the duodenal tube.

3. The insertion of the duodenal tube beyond the pyloric sphincter and movements of the intestine facilitate the decompression.

4. Decompression of the distended colon by means of suction applied to an inlying rectal tube is unsatisfactory owing to the sharply angulated flexures of the colon and to the more solid content of the lower bowel.

HERNIA INTO THE UMBILICAL CORD AND RELATED ANOMALIES

L. ALBERT THUNIG, M.D.
BROOKLYN

Hernia into the umbilical cord, or true congenital umbilical hernia, as the condition is now termed, is a comparatively uncommon anomaly. It is said to occur once in every 5,000 or 6,000 new-born infants.[1] Like all anomalies of embryonal development, in no two cases does it present exactly the same anatomic picture or the same surgical problem, although in a general way the manifestations are always similar. Furthermore, the chance that any one surgeon will see or operate on any large number of patients with uncommon anomalies is unlikely. Hence, the surgical procedures are as varied as the anatomic peculiarities and as the operative technics. For these reasons I believe that the case to be described here merits recording. The comments on closely related anomalies are based almost entirely on case reports in the literature and are given in order to emphasize by comparison or contrast the close relationship which exists. The drawings which I have copied illustrate this same point. The classification which I shall give will, I hope, bring under one heading several conditions that are undeniably closely related but which now appear in various classifications.

EMBRYOLOGY

In order to understand the occurrence of so-called hernia into the umbilical cord and other closely related anomalies, it is essential to have a clear understanding of some of the anatomic structures of the human embryo and their connection with the umbilicus and gastro-intestinal tract.

In a recent article Truesdale[2] has given a brief but clear description of some of the embryology concerned here, and I have taken the liberty of copying it. In the 5 mm. embryo the digestive tract consists of a tube which is closed at both ends and attached to the dorsal part of the mesentery, which extends from one end of the embryo to the other. By the time the embryo is 9 or 10 mm. in length the liver has grown so large that it diminishes the available abdominal space, and the

1. Milch, Henry: Adherent Congenital Umbilical Hernia, Am. J. Dis. Child. **42**:608 (Sept.) 1931.

2. Truesdale, P. E.: Retroposition of the Transverse Colon, J. A. M. A. **104**:1697 (May 11) 1935.

intestinal loop is extruded into the root of the celom of the umbilical cord (exocelom, or extra-embryonic celom), forming a physiologic hernia (fig. 1). At this stage, when the embryo is from 5 to 10 weeks old, the first rotation of the intestine takes place. While the intestine lies extra-abdominally (in the exocelom), the caudal limb lies to the left of the cephalic limb, and the small intestine assumes a position below and to the left of the colon. The colon assumes an inverted U shape and lies opposite the midline of the posterior abdominal wall.[3]

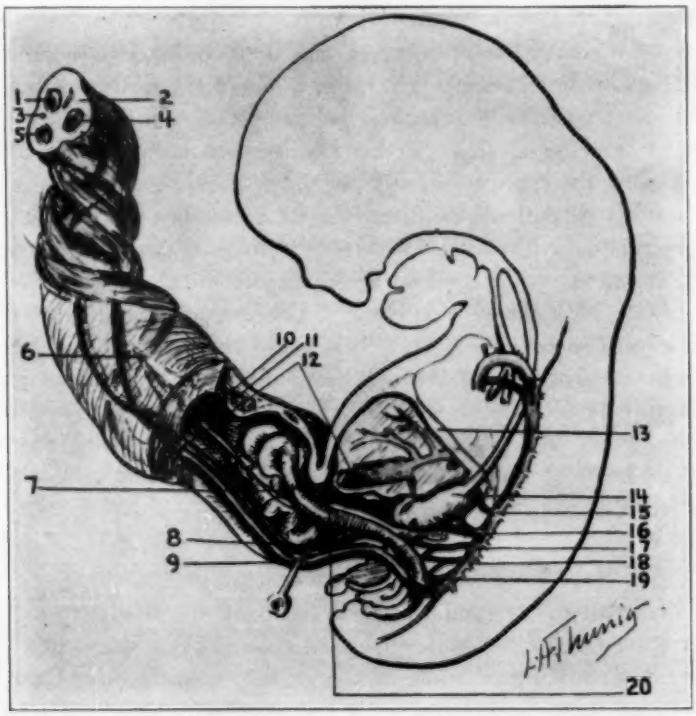

Fig. 1.—Human embryo, 23 mm. long. *1* and *5* indicate umbilical arteries; *2* and *10*, omphalomesenteric vessels; *3* and *8*, allantois; *4*, umbilical vein; *6*, distal end of the exocelom; *7*, colon; *9*, left umbilical artery; *11*, cystic spaces in the cord wall which denote beginning obliteration of the exocelom; *12*, umbilical vein (portion removed); *13*, diaphragm; *14*, stomach; *15* to *18*, phrenic, celiac, superior and inferior mesenteric arteries; *19*, right umbilical artery; *20*, point at which it is assumed that adhesions form in a so-called paraduodenal hernia. (Copied from the drawing by Max Brödel in T. S. Cullen's [7] textbook, page 11).

The second stage, which is the important time when the midgut loop is returned to the abdomen, occurs at the tenth week. The return

3. Bailey, F. R., and Miller, A. M.: Textbook of Embryology, ed. 4, New York, William Wood & Company, 1923, p. 305.

of the intestine to the abdominal cavity is due to a fall in the intra-abdominal pressure, which results from the increase of space within the abdomen; the extra-abdominal pressure pushes back the contents of the sac,[4] or, according to Broman,[5] the intestine is gradually sucked back into the abdominal cavity when the latter has grown sufficiently large. The intestine does not return *en masse*. The proximal limb returns first and occupies the lower part of the abdomen below the liver. Thus the small intestine passes to the left below the colon and mesenteric vessels. The colon retains its inverted U shape, but the upper limb of the U is pushed transversely by the small intestine below and the stomach and liver above. The cecum returns last. As this enterocolic loop reenters the abdominal cavity it undergoes torsion of 270 degrees counterclockwise about the axis of the superior mesenteric artery.[6]

The following facts are added, as they have an important bearing on the etiology of the anomalies to be discussed.

Authoritative Embryologic Facts.—1. The exocelom reaches its maximum size in the 30 mm. fetus, and the greater part of the small intestine develops in it[7] (fig. 2).

2. The exocelom is lined with peritoneum which is a continuation of the parietal peritoneum of the abdominal cavity (celom, or intra-embryonic celom[8]).

3. The omphalomesenteric duct, or vitalline duct, and its vessels are present in very early fetal life. They pass from a loop of small intestine through the exocelom to the yolk sac[7] (figs. 1 and 2).

4. Generally speaking, the omphalomesenteric duct disappears when the embryo is between 4 and 12 mm. in length, but its vessels persist long after the duct has disappeared.[7]

5. The intestine enters the abdomen about the third month.[7]

6. The exocelom disappears about the third month.[7]

7. The umbilical ring closes about the third month.[7]

8. The amnion is reflected along the cord and at the fetal end of the cord passes directly to the skin of the fetus. The point of transition

---

4. Bardeen, C. R.: Am. J. Anat. **16**:427 (Sept. 14) 1914.

5. Broman, I.: Normale und abnormale Entwicklung des Menschen, Weisbaden, J. F. Bergmann, 1911, p. 380.

6. Dott, N. M.: Brit. J. Surg. **11**:251 (Oct.) 1923.

7. Cullen, T. S.: Diseases of the Umbilicus, Philadelphia, W. B. Saunders Company, 1916.

8. Keith, Arthur: Human Embryology and Morphology, ed. 4, London, Edward Arnold & Co., 1921.

occurs from 0.5 to 1 cm. out on the cord and ends in a ring-shaped swelling.[9]

9. The adhesions which the ascending colon forms just before or after birth as the cecum assumes its final position in the iliac fossa are subject to a great range of variations, and many peritoneal folds and recesses may be formed. The purpose of all of them is to give fixation of the viscera to the abdominal wall.[8]

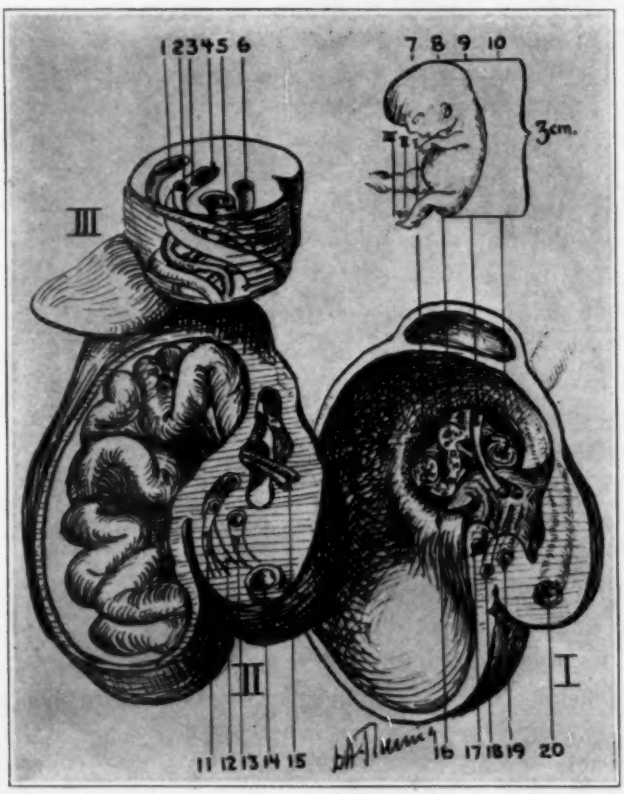

Fig. 2.—Human embryo, 3 cm. long, showing the structures of the umbilical cord. *1, 12* and *17* indicate right umbilical artery; *2, 11* and *18*, allantois; *3*, tip of exocelom with omphalomesenteric vessels inside; *4, 15* and *9*, omphalomesenteric vessels; *5, 14* and *20*, umbilical vein; *6, 13* and *19*, left umbilical artery; *7*, small intestine; *8*, mesentery of the small intestine; *10*, large intestine; *16*, umbilical ring at the base of the exocelom. *I, II* and *III* indicate the level at which the sections were made, as shown in the sketch of the embryo in the upper right hand corner of the figures. (Copied from the drawing by Max Brödel in T. S. Cullen's [7] textbook.)

---

9. Runge, H. M.: Die Wundinfectionskrankheiten der Neugeborenen, in Die Krankheiten der ersten Lebenstage, Stuttgart, F. Enke, 1893, p. 56.

REPORT OF A CASE

C. B. was born prematurely at the Prospect Heights Hospital at 10:20 a. m. on May 24, 1932, at eight and one-half months' gestation, by precipitate labor. He cried spontaneously. The weight was 3 pounds and 2 ounces (1,364 Gm.). The facies was mongoloid. I saw the infant immediately after birth, while the umbilical cord was still intact and the placenta undelivered.

Fig. 3.—Appearance at birth of a so-called hernia into the umbilical cord as viewed from the right side. The sac was cut away, as described in step 2 of the operation, along the cord from *A* to *B*.

The umbilical area presented the usual elevated collar of skin with a typical thin but well defined crenated edge (fig. 3). This collar of skin extended from ½ to ¾ inch (1.2 to 2 cm.) above the level of the abdomen and was not more than ½ inch (1.2 cm.) in diameter. A small but well defined umbilical cord occupied and was laterally attached to the upper angle of the collar of skin, and attached to the remainder of the circumference of the collar and going down into it was a thin, transparent membrane. From the collar this membrane spread outward on the cord to form a sac, which extended for about

3 inches (7.5 cm.) along the cord and was about 2 inches (5 cm.) in diameter. The cord did not present any twists and was practically straight from the collar to the distal end of the sac. At the neck of the sac, that is, at the collar of skin, the cord, though intimately attached to the sac, was sharply defined. The neck and base of the sac apparently consisted of amnion and peritoneum only. At the distal end of the sac the cord was not so well defined, and there was considerable fusing of the cord substance with the amnion and peritoneum. The vessels of the cord were not, however, spread out over the sac. The sac was not distended, in fact, it was extremely flaccid, nor was it completely filled, in spite of the fact that it contained the cecum with the appendix, a part of the ascending colon and what appeared to be the greater part of the small intestine. All these structures could be plainly seen through the wall of the sac. The cecum and ascending colon occupied the right and lower part of the sac, and the small intestine was to the left and reached a slightly higher level than the ascending colon and cecum. (Apparently the ascending colon had successfully rotated to the right of the small intestine, and that relationship did not change during operation.) I regret to state that I neglected to examine minutely that portion of the sac adjacent to the ascending colon to see whether any attempt at fixation had taken place, as might have been evidenced by the presence of adhesions or by the presence and location of the ileocolic vessels. Of course, it is possible that inspection might not have revealed the facts, as the parts were very small; the large intestine was about the size of a little finger, and the appendix was about ½ inch (1.3 cm.) long and less than ⅛ inch (0.4 cm.) in diameter. The diameter of the small intestine was about the same as that of cooked spaghetti. The intestine was not distended and was of good color.

Although I had some theoretical knowledge of the embryology of this anomaly, I had never before been confronted by the actuality. I decided to operate at once on the following grounds: 1. It was evident that the umbilical ring was very small, and it seemed probable that incarceration or strangulation might take place with the ingestion of food. 2. I believed that at least the distal part of the sac would dry up because of the large amount of cord substance present, just as the cord normally dries up, and that this would endanger life by rupture of the sac. (This opinion has been corroborated by the occurrence of such an event in at least two cases [Sanderson [10] and Carrington Williams [11]]). 3. It seemed impossible for the thin, fragile tissue of which the sac was composed to escape trauma or infection. (Peritonitis was present in one fatal case at the time of operation, two days after birth [12]).

Operation.—Operation was begun at 11 a. m. The cord had been tied a short distance above the distal attachment of the sac. No attempt had been made to reduce the intestinal hernia.

Step 1: An attempt was made to dissect the sac intact from the cord. This was obviously impossible, and the sac was entered at the distal end.

Step 2: The sac was then cut away from the cord by sharp dissection from the distal end to the collar of skin. No bleeding or vessels of the umbilical cord were encountered.

Step 3: The cecum and appendix presented themselves within the sac. The meso-appendix was well defined. A single ligature was placed around the appendix, and the meso-appendix and appendix were removed. The parts of the intestine maintained their relationship within the sac, and no difficulty was experienced in

10. Cullen,[7] p. 462.
11. Williams, Carrington: S. Clin. North America **10**:805, 1930.
12. Williams, Carrington,[11] p. 808.

keeping them there. A very brief, unsuccessful attempt was made to return the intestine to the abdominal cavity. The umbilical ring admitted the tip of the little finger and was apparently patent.

Step 4: A circular incision was carried around the collar of skin about 1/16 inch (0.15 cm.) or less from and parallel to the thin crenated edge and carried down to the peritoneum of the neck of the sac.

Step 5: The peritoneum could then be stripped away easily and quickly from the inside of the collar. Separation was carried down by blunt dissection until the inside of the abdomen was reached extraperitoneally.

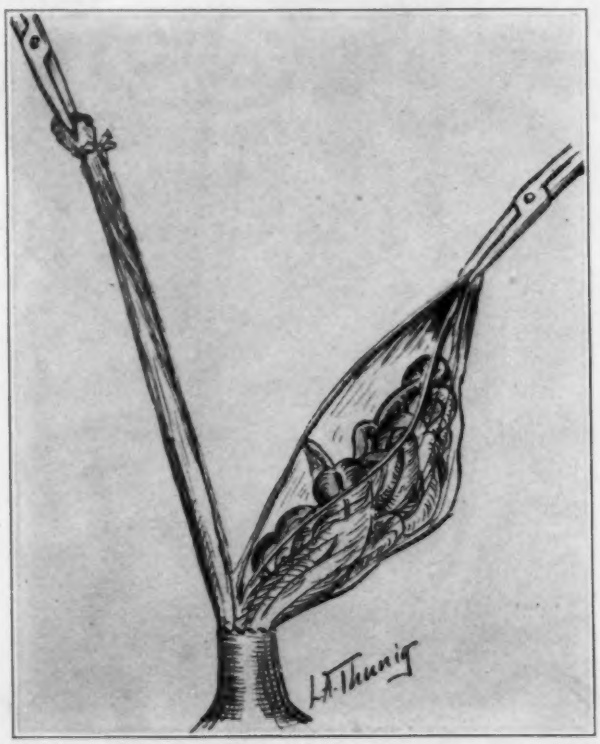

Fig. 4.—The appearance after the sac had been cut away from the cord at the conclusion of step 2. Step 3, removal of the appendix, was then carried out.

Step 6: Two incisions were then made, one above and one below the umbilicus. Each incision started at a median point on the cut edge of the collar; the collar was split, and the incision was carried along the median line of the abdomen for about 1 inch (2.5 cm.). The umbilical ring and the linea alba were split above and below the umbilicus down to the peritoneum. Still the intestine failed to return to the abdomen spontaneously, and it was left alone.

Step 7: The umbilical cord was then fixed by ligature and sutured to the cut edge of the linea alba above the site of the umbilical ring. The cord was cut so as to leave as short a stump as possible.

Step 8: The parietal peritoneum was separated by blunt dissection from the inside of the abdominal wall all around the opening, the immediate vicinity of the sutured stump of the umbilical cord being avoided. The base of the sac was then

spread out and was wide apart, with disappearance of the neck of the sac. The little ring of crenated skin had of course been severed when the umbilical cord was removed, and only a small remnant was left on the sac. The intestine still tended to remain within the sac, at least a considerable portion of it, particularly the large intestine.

Step 9: The opening of the sac was then closed with a continuous catgut suture, which was widely placed, with a good distance left between stitches. With the

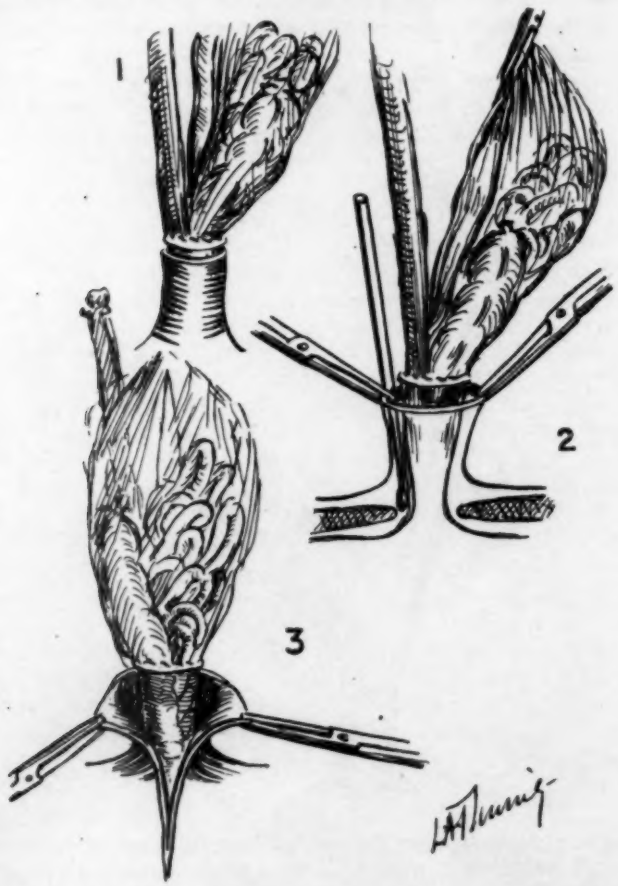

Fig. 5.—Operative steps 4, 5 and 6. Step 4 (at *1*), circular incision around the collar of skin, as viewed from the right side. Step 5 (at *2*), stripping the peritoneum away from the inside of the collar and carrying the separation into the abdominal cavity extraperitoneally. These views are from the right. Step 6 (at *3*), the incision is made below the umbilicus through the collar and then in the midline of the abdomen for about 1 inch (2.5 cm.), carried down to the peritoneum, splitting the linea alba and the umbilical ring. Exactly the same procedure was carried out above the umbilicus. This view is taken from below.

tightening and tying of this suture the size of the sac diminished markedly, and the sac and intestine were literally dropped into the abdomen.

Step 10: Because of the thinness of the abdominal wall and the minuteness of the parts, I deemed it unwise either to attempt suturing it in layers or to bury

any catgut in the tissues. The abdomen was closed with through and through Lembert silkworm gut sutures (peritoneum excluded) with as much overlapping as possible without tension. A few fine silk sutures were used for the skin.

The operation was completed at 11: 40 a. m. The anesthesia was negligible, as the child received only an occasional whiff of ether.

Progress.—The infant stood the operation well. No postoperative distention occurred, and the bowels moved spontaneously on the second day after operation.

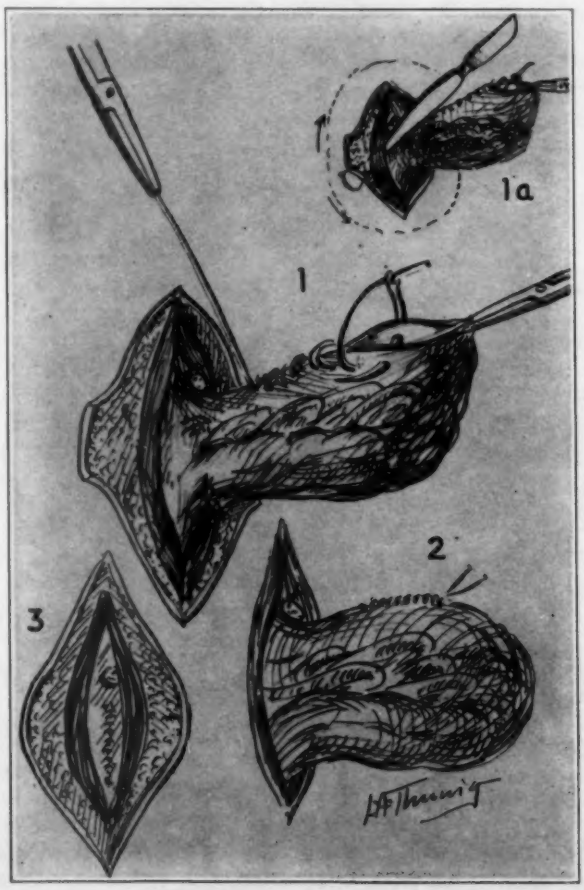

Fig. 6.—Operative steps 7, 8 and 9. *1*, step 7 has been completed, and the stump of the umbilical cord is sutured to the split linea alba. Step 8 (1a): Separation of the peritoneum from the abdominal wall by blunt dissection has also been completed, and the opening in the sac is being sutured. Step 9 (at *2*) shows the sac sutured, with a decrease in the size due to the pulling together of the widely placed continuous suture. *3*, showing the appearance at the completion of step 9, with the sac and its contents returned into the abdomen.

He nursed well at breast and was given also a supplementary formula, as the breast milk was deficient. He vomited only once postoperatively. The wound remained clean, and the sutures were removed on the sixth day. Shortly afterward an irregular slough developed at the upper angle of the wound. It involved only

the skin and was removed. Wide separation of the edges of the skin was prevented with an adhesive plaster strapping. The small stump of cord, however, made its way through the sloughed area. On June 2 the wound was clean, and the cord stump had separated. The infant was discharged on June 3, ten days postoperatively.

The temperature reached 101 F. within the first twenty-four hours after operation. Thereafter it did not rise above 100 F.

At birth the infant weighed 3 pounds and 2 ounces (1,364 Gm.). After a slight initial loss he gained progressively, and when 10 days old he weighed 4 pounds and 4 ounces (1,928 Gm.).

The nurses' report shows that in addition to one vomiting spell there was occasional regurgitation; otherwise the course was uneventful.

Fig. 7.—Photograph of abdomen of C. B., taken on July 8, 1935.

The child was seen by me after he was discharged from the hospital. The wound healed without difficulty, and the weight increased slowly. For several months after operation there appeared to be some weak, thin spots about the wound, without herniation. At 6 months there still remained one weak spot. In June 1935 the weak spots had disappeared, and there was no evidence of hernia. The abdominal wall was firm and presented the appearance shown in the photograph (fig. 7).

Roentgen Examination.—Being interested to know what influence the anomaly and/or its operative treatment might have on intestinal rotation, I had roentgenograms made.[13] The report, made by Dr. Charles J. Search, was as follows:

"On July 8, 1935, roentgenograms were made of the boy, aged 3 years and 2 months. They were made after the ingestion of a barium sulfate meal, together

13. It is an interesting sidelight to note the psychologic reactions of the parents of this infant toward a roentgen examination and also to note to what

(Footnote continued on next page)

with the giving of a barium sulfate enema, in order to show the size, shape and position of the stomach and large intestine. The plates show that the cecum is in the right iliac fossa, the ascending colon lies on the right side and the hepatic flexure is present. The transverse colon turns to the left on a level with the greater curvature of the stomach but, instead of rising to form the high splenic flexure, drops directly downward. At about the same level as the cecum on the right the transverse colon is reflected upward and, extending diagonally across the abdomen, forms what would normally be a splenic flexure but is really another hepatic flexure, which lies directly above the normal hepatic flexure. From this second hepatic flexure the descending colon arises and, following the course of the ascending loop of the transverse colon, passes diagonally downward and across the abdomen to the rectum and anus. The position of the different organs in the abdominal cavity as marked on the roentgenograms were carefully checked before and after the taking of the roentgenograms. The diagnosis is incomplete rotation of the transverse and descending colon."

Comment.—This report shows that the spreading out of the transverse colon across the upper part of the abdomen, with the formation of a splenic flexure and descending colon on the left, was incomplete. According to the best authorities this spreading out of the transverse colon is produced by the pressure of the small intestine from below and by the pressure of the stomach and liver from above. Thus, with the major part of the small intestine confined in the exocelom outside of the abdomen until after birth and in view of the fact that some visceral fixation had probably taken place by that time, one can readily understand the modus operandi in this case. This brings up the question of what bearing intestinal rotation and the behavior of the exocelom may have on one another. This is a lengthy topic, and I may say here only that in this case there was a definite relationship and the persistent extra-abdominal exocelom was the cause of the failure of the rotation. That this relationship also exists in cases of so-called paraduodenal hernia, which will be discussed later in this paper, has been definitely shown by Papez.[14] Whether faulty rotation is always due to the faulty behavior of the exocelom or vice versa or whether the actuating factor is variable is a question that is still unanswered.

In spite of this infant's early surgical experience and his present intestinal anomaly, he has been practically free from gastro-intestinal disturbances. He did not walk until he was 2½ years old, and he really does not talk as yet (July 1935).

---

extent one's enthusiasm and interest may influence one's actions. I sent the infant's father a letter explaining that I wished to have a roentgenogram made to determine the position of the intestine and volunteering to pay for it, as the family were in moderate circumstances. I fully expected an appreciative reply; instead I was notified that the child was well and did not need a roentgen examination; furthermore, the parents refused to have it made. In a spirit of foiled enthusiasm and resentment I drove rapidly to the home and found the mother, the infant and an older son. After much arguing and explaining I hustled the entire family into my car, rushed them to Dr. Search's office and obtained the roentgenogram. This explains why the barium was given by mouth and by rectum at the same time. It was an only opportunity and had to be seized. While the roentgenograms were being taken I learned that the parents believed that I was having the plates made so as to find some reason to operate again. Will the public ever learn that the physician sometimes thinks of something other than dollars and cents?

14. Papez, J. W.: A Rare Intestinal Anomaly of Embryonic Origin, Anat. Rec. **54**:197, 1932.

There is a hydrocele of the cord, which shows well in the photograph, and the mongolian type of facies that was noticeable at birth is now very marked and associated with imbecility or idiocy.

Criticism of the Operation Based on Embryologic Considerations, Operative Observations and Results.—Step 1: No comment is necessary.

Step 2: The lateral opening simplified the handling of the cord and the contents of the sac.

Step 3: The removal of the appendix was not justified, but the temptation was great and the risk seemed negligible in view of the simplicity of the procedure and the sterility of the gastro-intestinal tract. The fact that no difficulty was

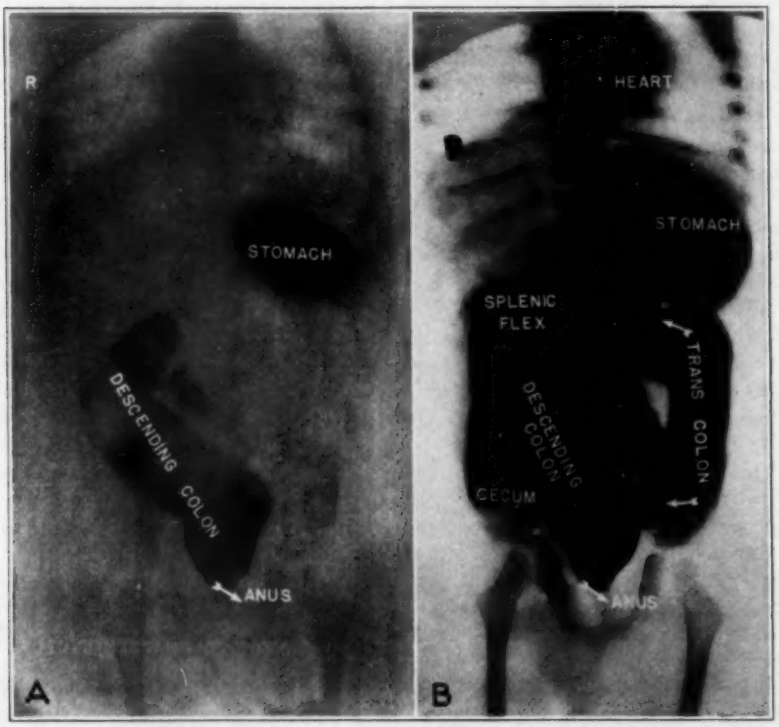

Fig. 8.—Roentgenograms of C. B., taken on July 8, 1935. A small amount of barium was given by mouth and by rectum to determine the intestinal capacity. *A*, the position of the descending colon and the beginning of transverse colon are well shown and make the interpretation of *B* much simpler. *B*, a roentgenogram taken immediately after the film shown in *B* (see text).

experienced in keeping the intestine within the sac, the failure of reduction within a patent umbilical ring and the maintenance of the intestinal relationship may have been due to any of four conditions: (1) a persistent omphalomesenteric duct, which is given as a cause for failure of reduction in at least three cases;[15] (2)

15. (*a*) Sheen, W.: Bristol Med.-Chir. J. **19**:310, 1901. (*b*) Fraser, John: Surgery of Childhood, Baltimore, William Wood & Company, 1926, pp. 774 and 776. Williams.[11]

possible attempt at fixation of the ascending colon to the base and neck of the sac; (3) an umbilical ring that was too small, and (4) simple adhesions. Frankly, I did not look for the omphalomesenteric duct, nor did I discover it by chance. I presume that showed negligence; but I was impressed with the fact that the ascending colon was the offending factor, and I still believe that it was. It has been shown that the lining of the exocelom is peritoneum which is continuous with the parietal peritoneum of the abdomen and that this exocelomic peritoneal sac may return to the general abdominal cavity during embryonic life.[16] It is only a fair assumption to believe that under normal conditions this exocelomic sac would spread out and become parietal peritoneum of the abdomen. Taking this probability into consideration with the fact concerning adhesions of the ascending colon, as given in this paper under the heading "Authoritative Embryonic Facts," makes me feel fairly certain that in this case there was some attempt at fixation of the cecum. At the time of operation I felt so certain that that had taken place and that the blood supply to the colon was involved in the base and neck of the sac that I believed the handling of the sac as any ordinary hernial sac might be handled would result in interference with the colonic blood supply and therefore concluded that it was imperative to reduce the sac, or part of it, with the intestine. This accounts for the technic used in the remainder of the operation.

That a too small umbilical ring was not the essential cause for failure of reduction is shown by the following steps: Simple adhesions may have been present.

Steps 4 and 5: This seemed to be the easiest way of establishing the identity of the peritoneum. The peritoneum stripped easily. There was also a direct approach to the umbilical ring.

Step 6: The failure of reduction with the ring split confirmed the opinion regarding fixation of the colon. This, of course, does not account for the failure of the small intestine to reduce, and it is possible that there was a persistent omphalomesenteric duct present which I overlooked or, possibly, simple adhesions, which are mentioned in one of the cases reported.[15a] I must say that my attempts at reduction were feeble, for I felt that handling or traumatizing the intestine was the one thing that should be avoided. I believe that the following out of this dictum was the most important factor in the uneventful recovery. In one case that has been reported in which reduction was difficult the child died of peritonitis three days after operation.[17] In Hope's case the small intestine was adherent to the sac but was easily separated. What the operators said they believed to be the appendix was intimately fused with the tissue of the cord and had to be ligated and cut off. Sheen [15a] gave as his opinion that it was a remnant of the omphalomesenteric duct.

Step 7: The cord was removed deeply with the idea of lessening the possibility of the development of an incisional hernia. The progress shows that the cord either should have been more radically removed or should have been disregarded, tied off in the usual manner after separation from the sac and allowed to take care of itself, as the stump actually did. Just how the cord was handled is not mentioned in many of the case reports. With cutting of the cord the small ring of crenated skin also was of necessity cut, and the small amount remaining on the sac was left in situ.

Step 8: This procedure was performed with the idea of widening the base of the sac, eliminating the neck of the sac and making the reduction of the sac

16. Mall, F. P.: Arch. f. Anat. u. Physiol., supp., 1897, p. 403. Jackson, C. M.: Anat. Rec. **3**:361 and 396, 1909. Papez.[14]

17. Powers, D'Arcy: Tr. Path. Soc. London **39**:108, 1888.

and intestine easy of accomplishment and without any constriction about the intestine. It successfully fulfilled all three requirements. The fact that even then the intestine did not slide into the abdomen strengthened the idea of intestinal fixation, already discussed.

Step 9: This step accomplished closure of the sac with a marked diminution in the size, thus again aiding the reduction *en masse*.

Step 10: This appeared to be the quickest, safest and easiest procedure by which to close the abdomen. The ultimate results justified it. Had it been realized at the outset that reduction of the contents of the sac independent of the sac was to prove nonsuccessful, then it would have been much better surgery to have commenced with step 4, followed by 5, 6, 2, 3, 7, 8, 9 and 10, in the order given.

COMMENT

It is generally agreed that operation for so-called hernia into the umbilical cord and amniotic hernia, which is to be described later, gives the best results if operation is performed soon after birth. The ability of the new-born to stand a major surgical procedure has been commented on by many. Freshman [18] confirmed these opinions and reported that in his case (in which there was a large amniotic hernia), operation was performed two hours after birth. He also stated that his search of the literature revealed the report of only one case in which operation was performed so soon after birth. McCaughan [19] reported a case of massive amniotic hernia in which operation was performed soon after birth, the appendix was removed and recovery followed. He, however, stated no definite time, and only meager details of the case are given. Reed [20] reported a case in which rupture of the sac and evisceration occurred under most unsanitary conditions. The infant was operated on two hours after birth; the appendix was removed, and recovery followed. Hernia into the umbilical cord does not seem to occur as commonly as amniotic hernia. Cases have been reported by Williams,[11] Fraser,[15b] Powers [17] and Sheen [15a] Haines and McIlroy [21] have reported an interesting case of amniotic hernia.

CLASSIFICATION AND NOMENCLATURE OF SO-CALLED HERNIA INTO THE UMBILICAL CORD AND CLOSELY RELATED ANOMALIES

Even in excellent and authoritative textbooks little has been written concerning these conditions, and the classification varies. In "Nelson's Loose-Leaf Living Surgery" there are about ten lines; Kelley [22] in his book entitled "Surgical Diseases of Children" gave about one page;

18. Freshman, Edgar: Lancet **2**:701 (Sept. 23) 1933.

19. McCaughan, J. J.: Memphis M. J. **10**:17 (March) 1935.

20. Reed, E. N.: Infant Disemboweled at Birth—Appendectomy Successful, J. A. M. A. **61**:199 (July 19) 1913.

21. Haines, C. E., and McIlroy, P. T.: Am. J. Surg. **21**:297 (Aug.) 1933.

22. Kelley, S. W.: Surgical Diseases of Children, New York, E. B. Treat & Company, 1909, p. 939.

Fraser [15b] in his book, "Surgery of Childhood" and Cullen [7] in his book entitled "Diseases of the Umbilicus" gave considerably more. In an article written as late as 1907 [22a] amniotic umbilicus is classified under tumors of the umbilicus. Williams,[11] following Cullen's classification, included under the heading of amniotic hernia a case of his own in which he stated there was no protrusion of the organs. Kelley classified them under the heading malformations of the linea alba and the umbilicus.[22] This was encouraging, but there the classification ended. Bearing these facts in mind I feel justified in suggesting a revised classification, even though it is only for the purpose of presenting the remainder of this paper in a systematic and anatomically orderly manner. I am fully aware that I am presuming greatly in this attempt at revision of the work done in many instances by masters, and it is with my humblest apologies that I offer my suggestions.

As a starting point I shall use Cullen's [23] classification. Under the heading of umbilical hernia Cullen gave the items in the following list but not in this order. For my convenience I have taken the liberty of changing his order as follows:

1. Umbilical hernia in the adult
2. Serous umbilical hernia
3. Cysts of the umbilicus
4. Small umbilical hernia at birth
5. Hernia into the umbilical cord
6. Congenital nipping off of a hernial protrusion
7. Amniotic hernia.

The first four of these groups can be excluded, as they do not represent anomalies and hence are not closely related to the present topic. The heading "cysts of the umbilicus" is not meant to include cystic conditions of the umbilicus associated with anomalies of the allantois or omphalomesenteric duct. These are, of course, true anomalies but belong to a classification apart from the one which I wish to emphasize, namely, anomalies dependent on the misbehavior of the exocelom. This leaves three items which are closely related, as I shall later show, and to these three I wish to add three more which, though mentioned in the literature, are not definitely classified. Under the present nomenclature the list is now as follows:

1. Hernia into the umbilical cord
2. Congenital nipping off of a hernial protrusion
3. Amniotic hernia

} From Cullen's classification

4. Amniotic umbilicus
5. Amniotic linea alba
6. Paraduodenal hernia, or retroperitoneal hernia

} From the literature

22a. Gallant, A. E.: Internat. Clin. **1**:151, 1907.
23. Cullen,[7] p. 459.

From an anatomic and embryologic etiologic standpoint these may be conveniently divided into four groups, as follows:

RELATED ANOMALIES OF THE UMBILICAL CORD, UMBILICUS, LINEA ALBA AND ABDOMINAL CONTENTS

Group I. Persistent extra-abdominal exocelom
- (*a*) With intestinal inclusion; patent umbilical ring (hernia into the umbilical cord)
- (*b*) With cutting off of the intestinal loop; umbilical ring usually closed (congenital nipping off of a hernial protrusion)

Group II. Persistent intra-abdominal exocelom with intestinal inclusion; return of the exocelom and intestine to the abdomen *en masse*
- (*a*) Before rotation of the ascending colon: right-sided persistent intra-abdominal exocelom with intestinal inclusion (right-sided paraduodenal hernia)
- (*b*) After rotation of the ascending colon; left-sided persistent intra-abdominal exocelom with intestinal inclusion (left-sided paraduodenal hernia)

Group III. Amniotic replacement of the deficient umbilicus and linea alba without visceral protrusion
- (*a*) Umbilical only—amniotic umbilicus (amniotic umbilicus)
- (*b*) Umbilicus and linea alba—amniotic linea alba (indefinite nomenclature)

Group IV. Amniotic replacement of a deficient linea alba with protrusion of the viscera into the hernia—amniotic hernia (amniotic hernia)

This list gives only six conditions, and I feel certain that there are others which are closely related to those that have been named. These will be briefly discussed. The case I have reported, in which there was incomplete rotation of the colon, tends to prove that there is at least some basis for suspecting that rotation of the intesine may be to some degree dependent on the time and the way the exocelom and its contents return to the abdominal cavity; or, if one prefers, the time and the way the exocelom and its contents return to the abdomen may be dependent on the rotation of the intestine. In the case reported it appears that the failure of rotation was due to the absence of the small intestine in the abdominal cavity. In the case of so-called paraduodenal hernia Papez [14] stated the opinion that the position, right or left, of the reduced exocelom depends on the time that the adhesions are formed with regard to the stage of rotation. Is it not quite as possible that the rotation or nonrotation of the intestine may depend on how and when the exocelom with its intestinal contents comes into the abdomen? I have mentioned these facts here to show that it is reasonable to believe that other anomalies will fall within the suggested classification. However, I shall confine my discussion to the six named.

In the following discussion I wish to give credit to those on whose work some of the nomenclature is based. Some of the arguments put forth hereafter have already been expressed, especially by Freshman.[18]

Persistent Extra-Abdominal Exocelom with Intestinal Inclusion (Hernia into the Umbilical Cord).—Mészáros [24] gave the name coeloma funiculi umbilicalis persistens to this condition. Freshman stated definitely that the present name is inaccurate. It is true that in the early embryo the initial intestinal tube is pulled or pushed into the exocelom, but that is a normal condition. The major portion of the small intestine actually grows in the exocelom; it has never been in the abdominal cavity. Hence, if it fails to enter the abdomen as it should and remains outside in the exocelom, I do not see how one can consider it a hernia in the strict sense of the term.

The case reported is an excellent example of so-called hernia into the umbilical cord, and the report brings out all the anatomic details. The relationship of the sac to the cord tissues and the amniotic cord covering may vary with the site of the exocelom. Cullen showed beautifully with drawings from the fetus that the exocelom may be centrally or laterally placed in the proximal end of the cord. Thus in one case the umbilical vessels were spread out over one side of the sac.[15a] A persistent omphalomesenteric duct has already been mentioned as a cause of failure of reduction, and consequently one must consider it an associated etiologic factor in the production of the anomaly. The same argument holds true regarding adhesions within the exocelom or at the umbilical ring.

Persistent Extra-Abdominal Exocelom with Cutting Off of an Intestinal Loop (Congenital Nipping Off of a Hernial Protrusion).—In this condition a loop of intestine of varying length may remain within the persistent extra-abdominal exocelom and be cut off from the intestine within the abdomen by a closing or narrowing of the ring or by adhesions across the ring. In these cases the proximal and distal ends of the intestine that are usually adjacent to the amputated loop terminate in blind ends within the abdomen.[25] It is obvious that the exocelom could not enter the abdomen and the intestine remain out.

When one considers the modus operandi involved in the production of what is called congenital nipping off of an umbilical hernial protrusion, one cannot help but wonder whether this same process is in some cases a factor in the production of congenital atresia or stenosis of the intestinal tract.

---

24. Mészáros, K.: Arch. f. klin. Chir. **158**:650, 1930.

25. Kern, T.: Ueber die Divertikel des Darmkanals, Inaug. Dissert., Tübingen, L. F. Fues, 1874.

In Ahlfeld's [26] case, described by Cullen,[27] the major part of the small intestine and a portion of the large intestine were outside of the abdomen and attached to the umbilicus by a thin pedicle. Is it not a fair assumption that there may have been some cases in which only the intra-abdominal defect was found and the real etiologic factor was missed, because of a complete separation from the body and loss of the amputated loop during delivery? Is it not a fair assumption also that in some cases the constriction of the intestine may not have reached the point of complete separation but had resulted only in atrophy with atresia or stenosis and then, owing to their decreased size, the intestinal loops may have entered the abdomen through the constricted umbilical ring? Certainly this does not seem improbable, particularly in that portion of the intestinal tract which normally occupies the exocelom in embryonic life. The catching of several loops at one time or successively could readily account for the multiple and separated areas of atresia or stenosis so frequently noted in these cases. Atresia or stenosis in that portion of the intestinal tract which does not normally occupy the exocelom, that is, the duodenum and hindgut, cannot be so readily explained. Yet how can one prove that the duodenum may not at times abnormally occupy also the exocelom? In that event, in the presence of a constricting umbilical ring or adhesions it might undergo atresia, stenosis or even amputation. This appears not impossible when one considers the anatomic nearness of the duodenum to the embryonic exocelom and umbilical ring. It is rather noteworthy that the hindgut, atresia or stenosis of which cannot readily be explained by this theory, is, according to J. Fraser,[15b] uncommonly the seat of errors.

In view of the fact that Ahlfeld reported the case previously mentioned in 1873, it is likely that other writers have entertained the same opinions that I have expressed or similar ones, and in all probability a thorough search of the literature would show this to be true. Nevertheless, I have been unable to find a textbook or article which indicates it. The nearest I discovered was in an article by Fritz Laessing,[28] who mentioned Ahlfeld, Strang and Nahrath as supporters of the theory that an abnormal pull of the omphalomesenteric duct on the intestine in the exocelom is an important factor in the production of atresia and stenosis of the intestine. Laessing then ruled out their theory on the ground that the duodenum and part of the colon never occupy the exocelom and that multiple atresias or stenoses could not be explained on that basis.

---

26. Ahlfeld: Arch. f. Gynäk. **5**:230, 1873.

27. Cullen,[7] p. 464.

28. Laessing, Fritz: Arch. f. Kinderh. **97**:1, 1932.

I have already stated that to me it seems possible that the duodenum might under abnormal conditions occupy the exocelom. Laessing,[28] in his discussion of intestinal atresia, etc., stated the belief that the duodenum or terminal part of the colon never occupies the exocelom. Aeby [29] reported a case, with excellent photographs, and referred to four similar cases of a diverticulum of the heart in a child with so-called hernia into the umbilical cord. In this case the base of the hernia was about the size of a spectacle lens. The hernia contained small intestine and a pulsating mass, both of which were covered by the usual transparent membrane. The pulsating mass was about 1 cm. in diameter. The child lived three hours. Postmortem examination revealed that the pulsating mass was the end of a diverticulum of the heart and was connected with the heart proper by a pedicle of heart muscle about the thickness of a lead pencil. The heart occupied its normal place in the thoracic cavity and was, other than the diverticulum, normal. Although no definite bands were found, the author concluded that some must have existed some time in early fetal life.

Certainly if the development and behavior of the exocelom are such as to allow, under abnormal conditions, a portion of the heart to enter the exocelom and then to hold it there by means of adhesions or other factors with such force as to produce a diverticulum, as described in the case just mentioned, it seems only logical to believe that abnormally the duodenum, the later end of which normally occupies or is in close proximity with the exocelom, and the hindgut, the continuity of which normally occupies the exocelom, might both readily get into the exocelom and, once in there, might under continued abnormal development be ensnared with resulting atresia, stenosis or amputation. It has been demonstrated in actual cases that intestinal loops normally in the exocelom have been amputated. Then why not amputation of intestinal loops accidentally occupying the exocelom? One thing is certain, and that is that the fact that the duodenum and hindgut do not normally occupy the exocelom is not sufficient evidence in itself to prove that accidents of the exocelom can be absolutely ruled out as an etiologic factor in intestinal atresias, stenoses and amputations including the duodenum and the hindgut.

Certainly there must be other etiologic factors in some cases of intestinal atresia and stenosis, but to me it seems not improbable that in some cases the anomaly is etiologically closely related to congenital nipping off of an umbilical hernial protrusion.

Persistent Intra-Abdominal Exocelom with Intestinal Inclusion.—The following material is abstracted and quoted from a paper by James Papez entitled "A Rare Intestinal Anomaly of Embryonic Origin." [14]

29. Aeby, H. Koller: Arch. f. Gynäk. **82**:184, 1907.

According to Moynihan and others, paraduodenal hernia is believed to be due to the intrusion of a loop of small intestine into one of the nine peritoneal fossae which occur near the duodenojejunal flexure or in relation to the mesenteries.[30] Andrews [31] disagreed most emphatically with this conception, however, for the following reasons:

1. A differential pressure is utterly lacking; the pressure in the main cavity can never be higher than the pressure within the pouch. No vis a tergo to account for the formation or growth of such a hernia is present.

2. There are literally hundreds of similar folds and fossae in the peritoneum, many of which are larger, and they are practically never the sites of such hernias.

3. In all but a small number of the cases reported the degree of herniation has been total or subtotal. How can one conceive of a force which would, once begun, practically always continue to act until the intestine had been segregated into a sac, even when the rest of the abdomen was empty?

Andrews concluded that so-called paraduodenal hernia is a congenital anomaly due to the imprisonment of the small intestine beneath the mesentery of the developing colon. Papez did not give as his belief that even this is adequate to account for all the conditions usually seen. Papez, who based his deductions on a condition observed at autopsy (fig. 9), stated the opinion that what corresponds to paraduodenal hernia is due to an exocelom which, with its intestinal contents, is drawn en masse into the general abdominal cavity by adhesions at the abdominal orifice of the exocelom to the duodenum (fig. 1, 20; the entire small intestine from the duodenum on is normally found in the exocelom together with part of the large intestine). The exocelom then persists within the abdominal cavity. With the increase in size of the intestine the exocelom increases proportionally. In his case the linea alba was normal and the umbilicus was closed, so apparently only the peritoneal lining of the exocelom with the intestinal inclusion was pulled into the abdomen. The reason the cecum was not in the sac, Papez stated, was that the adhesions involved only the duodenum and its mesentery. He gave as his opinion that the position of this exocelom with its intestinal inclusion depends on the time at which the adhesions between the duodenum and the orifice of the sac developed. If adhesions formed before the rotation of the ascending colon to the right and thus pre-

30. Moynihan, B. G. A.: On Retro-Peritoneal Hernia (Being the Arris and Gale Lectures on the Anatomy and Surgery of the Peritoneal Fossae), ed. 2, New York, William Wood & Company, 1906.

31. Andrews, E.: Surg., Gynec. & Obst. **37**:740, 1923.

vented it, the sac would of necessity come down on the right of the ascending colon and be suspended from the duodenum (figs. 9 and 10). If the adhesions did not form until after the rotation of the ascending colon, the sac would come down to the left of the ascending colon (fig. 11). These conditions he said correspond to so-called right and left paraduodenal hernias or retroperitoneal hernias. In 139 cases of paraduodenal hernia, 34 hernias were on the right and 105 on the left.[32]

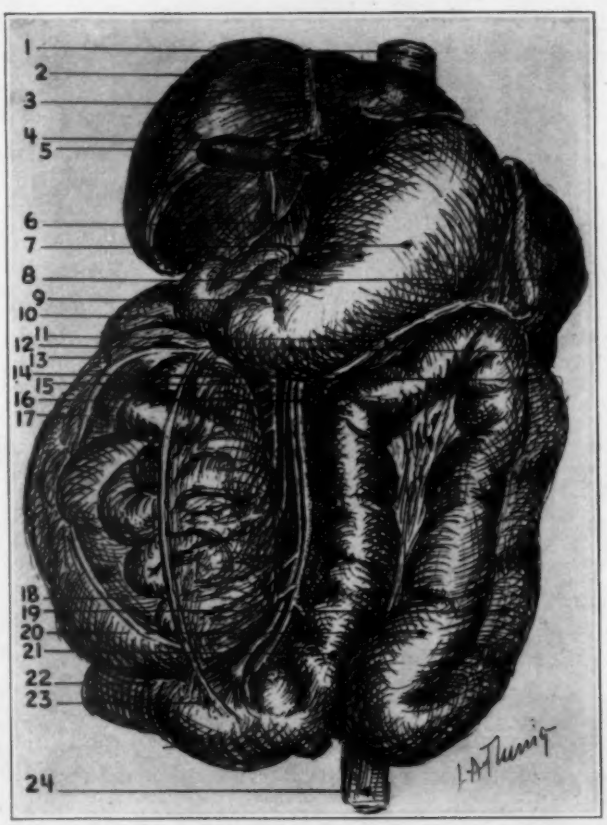

Fig. 9.—Copy of a drawing from actual case described by Papez [14] as an instance of a "rare intestinal anomaly of embryonic origin." By inference from the text there was a so-called right paraduodenal hernia or retroperitoneal hernia. I take the liberty of calling it a persistent intra-abdominal exocelom with intestinal inclusion. *1* indicates the esophagus; *2*, liver; *3*, falciform ligament; *4*, round ligament; *5*, gallbladder; *6*, hepatoduodenal ligament; *7*, stomach; *8*, spleen; *9*, pylorus; *10*, duodenum; *11*, cut edge of the omentum; *12*, kidney; *13*, sac (peritoneal lining of exocelom); *14*, splenic flexure; *15*, mesenteric vessels; *16*, ileocolic vessels; *17*, jejunum; *18*, ileum; *19*, transverse colon; *20*, transverse colon; *21*, ascending colon; *22*, cecum; *23*, adhesions; *24*, pelvic colon.

32. Dowdle, E.: Surg., Gynec. & Obst. **54**:246, 1932.

The argument put forth by Andrews [31] as to the improbability of the old conception of paraduodenal hernia is so strong and the actual anatomic findings and the deductions made therefrom by Papez are so convincing that to me the later conception seems more plausible, and I have accordingly included it under the same heading as hernia into the umbilical cord. If Papez was correct, it is evident that in reality paraduodenal hernia is not a hernia. Furthermore, it brings so-called paraduodenal hernia and so-called hernia into the umbilical cord into close relationship. In one instance, there is a persistent exocelom with intestinal inclusion outside the abdomen; in the other, it is within the abdo-

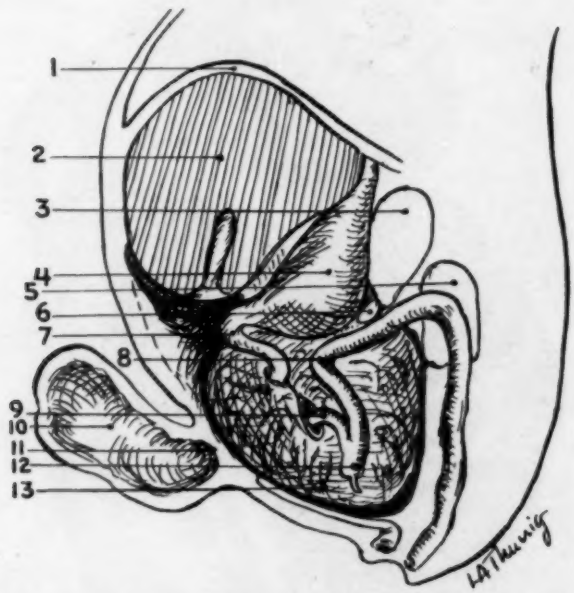

Fig. 10.—A copy of a diagrammatic sketch from the article by Papez [14] representing the formation of so-called right paraduodenal hernia. The ascending colon has not rotated to the right. *1* indicates the diaphragm; *2*, liver; *3*, adrenal glands; *4*, stomach; *5*, kidney; *6*, spleen; *7*, duodenum; *8*, colon; *9*, ileum; *10*, exocelom minus a peritoneal lining; *11*, umbilical opening; *12*, cecum; *13*, sac. The peritoneal lining of the exocelom with the intestinal inclusion has been reduced *en masse* from the umbilical cord, resulting in a persistent intra-abdominal exocelom with an intestinal inclusion. The colon is unrotated. (The position of the transverse and descending colon would probably differ from this sketch and be as shown in figure 9.)

men. If the foregoing statement is correct, the two conditions just cited are the two extremes of this particular type of anomaly; and if that is so, it is only a fair assumption that there must be some cases in which the anomaly has been arrested at some stage between the two extremes. Possibly the future will demonstrate that fact. There must

also be variations, depending on whether the exocelom is empty or full, whether the umbilical ring is open or closed and whether or not the intestine is rotated. These are purely theoretical assumptions at present.

It was by the merest chance that I stumbled on the illuminating paper by Papez, for its title would not ordinarily include it in the list of references to be consulted concerning hernia into the umbilical cord. Furthermore, it appeared in a strictly scientific journal which would be less likely to be consulted than a clinical journal. It is for this reason that I have taken the liberty of quoting freely from the article and have

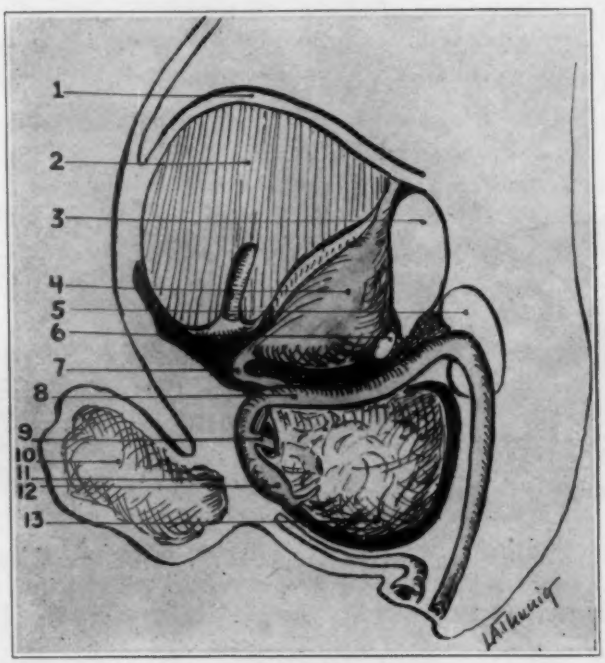

Fig. 11.—A diagrammatic drawing from the article by Papez[14] representing the formation of a so-called left paraduodenal hernia. The colon has rotated to the right. *1* indicates the diaphragm; *2*, liver; *3*, adrenal gland; *4*, stomach; *5*, kidney; *6*, spleen; *7*, duodenum; *8*, colon; *9*, ileum; *10*, exocelom wall minus its peritoneal lining; *11*, umbilical opening; *12*, cecum; *13*, sac. The lining of the exocelom with the intestinal inclusion has been reduced *en masse* from the umbilical cord, forming a persistent intra-abdominal exocelom with an intestinal inclusion.

attempted to copy his drawings, so that so-called paraduodenal hernia may be linked up with other anomalies of the exocelom, which I believe was the intention of Papez, even though he did not comment specifically on that point.

Amniotic Umbilicus.—In this condition there is a closing defect of the umbilical ring, and the deficiency is closed in with amnion reflected

from the cord. In at least one case there was a well defined ring at the umbilical site covered by a thin disk of fused amnion and peritoneum. The ring and disk became converted into scar tissue, and the umbilicus healed without difficulty.[33]

Amniotic Linea Alba.—This condition has heretofore not been given any specific name but has been described as a type of amniotic hernia, although it may exist without actual hernia. As the name implies, there is a deficiency of the linea alba with amniotic replacement, which may vary from a small area to practically the entire anterior abdominal wall. That it may exist without protrusion of the viscera has been shown by one case, Carrington Williams',[11] in which there existed in a 2 day old Negro child a congenital deficiency about the umbilicus about 3 inches

Fig. 12.—A sketch (with artist's liberties) of the photograph of an infant with an amniotic hernia (the case reported on by Dr. H. Wellington Yates), as shown in Cullen's [34] textbook entitled "Diseases of the Umbilicus."

(7.5 cm.) in diameter. This was covered by a transparent membrane, through which the intestine could be seen; but there was no protrusion.

Amniotic Hernia.—In this condition there is a primary amniotic linea alba with secondary actual herniation. Not only intestine but parts of or entire organs which normally develop within the true abdominal cavity have been found in these hernias. These are true hernias and may progress after birth.[34] Several references covering cases of amniotic hernia have already been cited.

---

33. Nicaise, E., in Dictionnaire encyclopédique des sciences médicales, Paris, V. Masson & fils, 1881, vol. 15, p. 140. Tordens: Clinique, Bruxelles **111**:353, 1889.

34. Cullen,[7] p. 462.

SUMMARY

Case Report.—It is shown that even a premature infant, weighing 3 pounds and 2 ounces (1,364 Gm.), forty minutes after birth may stand a major surgical procedure well, and with a condition such as was present immediate operation offers the best chance for recovery.

In this case certain conditions, not definitely determined, prevented reduction of the intestine into the abdomen even when no restricting ring of any kind was present.

The choice of overcoming this failure at reduction lay between removing the cause, with consequent handling of the intestine, or reducing the intestine in the sac. The latter method was chosen, and the postoperative course was smooth, with no gastro-intestinal disturbance immediately or during the following three years. A roentgenogram made when the child was 3 years old showed that the cecum was in the normal position.

The roentgenogram showed also an incomplete rotation of the transverse colon and upper end of the descending colon. This brings up the important question of the relationship of the normal or abnormal behavior of the exocelom and its contents and the process of intestinal rotation; also the determination of whether the abnormal behavior of the exocelom and its contents is the primary factor in the abnormal rotation, or at least some phases of it, or vice versa. To the best of my knowledge a roentgenogram has never been made in connection with such a case.

Nomenclature and Classification.—The present nomenclature is inaccurate. It does not give an insight into the actual anatomic or embryologic etiology of the conditions.

The nomenclature which is suggested, though rather wordy, does apply to the conditions named on an anatomic basis.

The classification, though possibly incomplete, covers the six conditions named and groups them in a systematic and anatomically orderly fashion.

The classification, irrespective of its merits or demerits, cannot be other than helpful to those seeking information in the literature on the six conditions included, which are shown to be closely related anomalies.

QUANTITATIVE STUDIES ON CONGENITAL CLEFTS OF THE LIP

WILLIAM T. PEYTON, M.D.
AND
HARRY P. RITCHIE, M.D.
MINNEAPOLIS

Previous studies [1] indicate that cleft palate consists not of an underdevelopment of tissue but of an abnormal displacement of the fully developed parts of the palate. It was also demonstrated that there is no tendency for the deformity to increase after birth. Measurements of the faces of children with clefts of the lip were so taken as to indicate the position of various parts of the nose in regard to the tragus of the ear and the position of the margins of the clefts in regard to the tragus. An analysis of these measurements is here reported.

This investigation was made to determine how much displacement of tissues had occurred in these children and also to find if such displacement is modified with age on account of unequal growth or continued unopposed muscle pull.

The measurements were made on the same children whose palates were previously measured,[1] i. e., ninety-one normal children and fifty-seven children with congenital clefts of the lip and palate. The cleft was bilateral in fourteen and on the left side in twenty-six and on the right side in seventeen.

The measurements analyzed in this paper are indicated in the accompanying illustration. They were taken from the tragus of the ear to the midline of the upper lip in the normal child and to the edge of the cleft in the maldeveloped child; in both the normal and the maldeveloped child the measurements were made from the tragus of the ear to the side of the nose, from the tragus of the ear to the midline or tip of the nose and from the tragus of the ear to the nasion, respectively.

From the Department of Surgery of the University of Minnesota.

Aided by a grant from the Graduate School Fund for Medical Research, University of Minnesota.

1. Peyton, William T.: Dimensions and Growth of the Palate in the Normal Infant and in the Infant with Gross Maldevelopment of the Upper Lip and Palate, Arch. Surg. **22**:704-737 (May) 1931; Dimensions and Growth of the Palate in Infants with Maldevelopment of the Upper Lip and Palate, Am. J. Dis. Child. **47**:1265-1268 (June) 1934.

Regressive lines, $y = a - bx$, have been fitted by the pearsonian correlation technic to the data for each dimension and the crown-heel length,[2] the material being divided into the following categories:

1. Bilateral cleft lip and palate
   (*a*) Data for left side
   (*b*) Data for right side
2. Cleft of lip and palate on left side
   (*a*) Data for left side
   (*b*) Data for right side
3. Cleft of lip and palate on right side
   (*a*) Data for left side
   (*b*) Data for right side
4. Normal lip and palate
   An average of the measurements of the left and right sides was used
5. All unilateral clefts of the lip and palate
   (*a*) Measurements on the cleft side
   (*b*) Measurements on the noncleft side

The results of comparison of the means and the coefficients of regression (b[3]) are given in table 2. The regression coefficient (b) is the slope of the line, and therefore it measures the rate of increase with an increase in the crown-heel length. A significant difference in the coefficients of regression would indicate that the rate of growth is not the same. However, in none of these comparisons of the regression coefficients is P less than 0.16, which means that there are in no two groups compared more than sixteen chances in a hundred that a true difference in rate of growth occurs.

Since the rates of growth are the same, the midpoint of the regression lines or the means for the various groups may be used to compare the actual size of each dimension. Such a comparison demonstrates that all the measurements taken are shorter in the child with a cleft of the lip and palate. That there is not a significant difference in the size of the head in relation to the length of the body between the normal child and the child with a cleft has been previously demonstrated.

Although there is no significant difference in the measurements for the right and the left side of the normal child or of the child with bilateral cleft of the lip, still the averages for the left side are smaller in every case except one, the average for the left auriculolabial measurement in the normal child being slightly longer. This might be due to some constant error in the technic of taking these measurements. The number of measurements is too small to be conclusive, but it is sug-

2. The statistical analysis was done under the direction of Dr. Edith Boyd, of the Department of Anatomy.

3. $b = \gamma_{xy}\frac{\sigma_y}{\sigma_x}$ $a = y + \sigma_x$

TABLE 1.—*Results of Measurements on One Hundred and Forty-Eight Children*

Crown-Heel Length, Cm.	Age, Days	Auriculo-Alveolar Measurement, Cm.		Auriculonasal (Side) Measurement, Cm.		Auriculonasal (Midline) Measurement, Cm.		Auriculonasion Measurement, Cm.	
		Left	Right	Left	Right	Left	Right	Left	Right
A. Normal Children									
45.7	10	7.7	7.3	6.7	6.8	8.0	8.1	7.8	8.2
48.8	12	8.0	7.5	7.2	6.9	8.7	8.1	8.1	8.3
49.0	2	...	...	7.1	7.4	8.5	8.4	8.0	8.2
49.2	1	9.0	9.1	7.7	7.3	9.1	9.0	8.9	8.5
49.3	16	8.5	8.4	7.3	7.3	8.5	8.5	8.3	8.3
49.3	10	8.6	8.9	7.8	7.8	8.9	9.2	8.7	8.3
50.0	29	8.0	8.0	6.7	6.6	7.8	7.9	8.3	8.1
50.2	3	...	...	7.1	7.1	8.5	8.3	8.5	8.4
50.4	10	8.1	8.9	6.9	7.6	8.1	8.8	8.1	8.2
51.5	4	8.5	8.5	7.3	7.6	8.6	9.0	8.6	8.9
51.7	16	8.4	9.0	7.5	7.5	9.0	9.2	8.4	8.9
51.8	10	8.5	8.3	7.4	7.4	8.8	8.7	8.5	8.5
52.1	14	9.0	8.9	7.5	7.7	9.2	9.0	8.8	8.8
52.5	40	8.5	9.0	7.5	7.8	9.0	9.0	9.0	9.0
52.6	53	8.0	8.2	7.4	7.2	8.6	8.8	8.5	8.4
52.7	0	8.8	8.9	7.6	7.4	9.3	9.3	8.8	8.7
52.7	66	8.6	8.3	7.3	7.3	9.0	9.0	...	...
52.9	6	8.2	8.4	7.0	7.2	8.6	8.7	8.3	8.3
53.1	35	9.3	9.1	7.8	7.8	9.3	9.1	9.7	9.1
53.1	32	8.7	8.9	7.6	7.7	8.9	9.0	9.0	9.0
53.4	5	9.0	9.5	8.3	8.2	9.4	9.8	9.2	9.2
53.7	66	8.6	9.1	7.6	7.6	9.2	9.3	8.9	9.6
54.2	20	8.5	8.8	7.4	8.0	8.8	9.3	8.5	9.2
54.3	36	9.5	9.2	8.2	8.0	10.1	9.4	10.6	9.3
54.6	37	9.7	9.5	8.5	8.5	9.8	10.0	9.5	10.1
55.2	36	9.0	8.6	8.5	7.6	9.5	8.7	9.0	8.5
55.4	47	8.2	8.1	7.5	7.9	9.2	8.7	9.5	9.5
55.6	60	9.6	9.1	8.5	8.5	9.1	9.5	9.7	9.5
56.1	63	9.5	9.6	8.5	8.5	9.5	9.2	9.1	9.0
56.3	158	9.2	9.0	8.5	8.4	9.5	9.6	9.2	9.3
56.3	68	9.5	9.5	8.3	8.4	9.8	10.0	9.8	9.8
56.6	48	8.8	9.0	7.7	7.8	9.5	9.2	9.3	9.3
56.8	86	9.5	9.7	8.5	8.5	10.0	10.5	9.4	9.9
57.3	51	9.9	9.9	8.4	8.5	10.2	10.0	9.1	9.4
57.5	91	10.2	9.7	8.0	8.5	10.0	9.8	9.6	9.8
57.9	83	10.1	9.9	8.8	8.7	10.0	10.1	9.7	9.6
57.9	87	9.0	9.3	7.8	8.2	9.4	9.6	9.7	9.2
58.2	82	10.0	10.0	8.8	9.4	10.3	10.2	10.3	10.5
58.5	85	9.5	10.0	8.9	8.9	9.6	10.2	10.0	10.0
58.7	83	9.7	9.2	8.9	8.5	9.6	9.8	10.0	10.0
58.9	124	10.3	9.7	8.9	8.2	10.5	10.2	10.0	10.0
59.0	119	9.7	9.5	8.6	8.2	10.1	9.6	9.1	9.5
59.0	136	9.0	9.2	7.9	8.0	9.0	9.1	9.4	9.3
59.0	75	9.0	9.0	8.1	8.0	10.0	9.8	9.6	10.0
59.3	45	9.9	9.9	8.8	8.7	10.0	10.2	9.9	10.0
59.5	143	9.8	9.8	8.9	8.5	10.5	10.0	10.3	9.8
59.9	105	10.3	10.2	8.8	8.8	10.6	10.6	10.8	11.0
60.1	113	9.1	9.0	8.4	8.0	10.0	9.6	10.0	9.4
60.3	99	8.6	9.4	8.3	8.4	9.6	9.5	9.3	9.6
60.4	101	10.0	10.2	8.6	8.8	9.5	10.1	9.5	9.5
60.5	93	9.6	9.4	8.3	8.2	10.0	10.0	10.2	10.2
60.5	79	9.8	9.6	8.6	8.4	9.8	9.8	....	....
60.8	106	9.8	9.5	8.9	8.4	9.9	9.5	9.3	9.4
61.0	152	10.2	10.5	9.0	9.2	10.5	10.7	10.1	10.3
61.1	90	9.6	9.7	8.2	8.4	9.8	10.1	9.3	9.2
61.7	134	9.0	9.2	8.5	8.5	9.5	9.5	9.0	9.6
61.7	140	10.0	10.0	7.0	8.0	10.0	10.5	...	...
61.8	162	9.8	9.9	8.4	8.8	9.4	9.8	9.3	9.9
61.9	109	9.9	9.8	8.4	9.0	10.0	10.5	10.1	10.0
62.0	68	9.5	9.3	8.2	8.4	9.8	9.9	9.5	9.6
62.7	115	9.5	9.5	8.4	8.4	10.0	10.1	10.0	9.8
62.9	141	9.8	10.0	9.3	9.5	10.5	10.2	10.5	10.2
63.6	123	10.3	9 6	8.8	8.2	10.2	9.8	9.5	9.4
63.7	176	10.9	10.6	8.8	9.5	10.3	10.5	10.0	10.0
64.1	135	9.6	9.8	8.5	8.5	10.6	10.1	10.3	10.5
64.4	259	11.0	11.0	9.0	9.4	10.6	10.9	11.2	11.2
64.5	100	9.9	10.0	8.9	8.9	10.0	10.2	10.5	10.5
64.8	203	11.0	10.5	9.8	9.7	10.8	11.1	11.0	11.3
65.1	219	10.3	10.7	9.2	9.4	10.6	10.8	11.0	11.0
65.7	198	10.2	10.0	9.0	9.0	10.4	10.0	9.9	10.1
65.7	141	10.5	9.8	9.4	8.5	11.0	10.2	11.0	11.3
65.7	213	9.5	9.5	8.1	8.4	9.7	10.5	10.0	10.1
66.6	168	10.2	10.5	8.9	9.3	10.1	10.8	10.5	11.0
66.8	225	10.6	11.1	9 2	9.3	10.6	11.3	10.5	11.0
66.9	241	10.1	10.1	9.0	8.8	10.2	10.0	10.2	10.5
67.0	179	10.0	10.0	9.3	9.1	10.2	10.5	10.0	10.0
68.0	286	10.5	10.1	9.0	9.2	10.2	10.6	10.5	10.2
68.0	325	10.5	10.2	8.8	9.1	10.3	10.4	10.3	10.3
68.2	188	9.3	10.4	8.4	9.0	10.0	10.6	9 2	10.2
68.5	278	10.2	10.0	9.0	9.0	10.4	10.0	10.0	10.2

TABLE 1.—*Results of Measurements on One Hundred and Forty-Eight Children—Continued*

Crown-Heel Length, Cm.	Age, Days	Auriculo-Alveolar Measurement, Cm.		Auriculonasal (Side) Measurement, Cm.		Auriculonasal (Midline) Measurement, Cm.		Auriculonasion Measurement, Cm.	
		Left	Right	Left	Right	Left	Right	Left	Right
69.0	313	10.5	10.5	9.2	9.0	11.0	11.0	11.1	11.2
69.1	283	9.6	9.5	9.2	9.0	10.0	10.5	10.5	10.5
69.3	238	10.5	10.0	9.0	9.0	10.8	10.3	11.5	10.0
70.0	272	10.0	10.0	9.0	8.4	10.4	10.2	10.4	10.5
70.2	238	9.9	9.8	7.8	8.2	10.2	10.0	10.5	10.2
70.7	282	10.4	10.4	9.0	8.9	10.5	10.4	10.4	10.0
71.5	344	10.3	10.5	9.5	9.0	10.5	10.2	10.3	10.7
72.5	330	10.6	10.5	9.7	9.3	11.0	11.2	10.6	10.5
73.8	315	10.6	10.8	9.5	9.3	10.5	11.0	10.5	11.1
75.4	259	11.2	11.2	9.5	9.5	11.2	11.5	11.2	11.3
75.5	362	11.0	11.0	9.8	10.0	11.5	11.1	11.1	11.2
				B. Maldeveloped Children					
				1. Bilateral Clefts					
47.5	11	7.2	7.2	7.1	6.7	8.8	8.8	8.2	8.5
50.3	3	7.2	7.1	6.8	6.7	8.6	8.5	8.5	8.5
52.1	28	7.4	7.4	7.1	7.0	8.9	8.9	8.7	8.7
52.3	25	7.1	7.1	7.0	6.9	8.7	9.0	8.9	8.8
52.7	46	7.6	8.1	7.3	7.6	8.7	9.5	8.6	9.3
52.8	72	7.4	7.4	7.0	7.2	8.7	9.1	8.8	9.1
53.0	52	7.9	7.5	7.1	7.3	9.0	8.5	8.7	8.5
53.7	43	7.3	8.0	7.0	7.2	9.1	9.0	8.8	9.1
54.0	30	8.0	7.5	7.5	7.2	9.6	9.6	9.5	9.5
55.0	18	8.0	7.5	7.5	7.2	9.6	8.6	9.0	8.8
56.6	52	7.5	8.2	7.1	7.5	9.1	9.2	9.2	9.5
57.5	95	7.6	8.2	9.1	7.5	9.0	9.5	9.5	9.5
58.5	67	9.0	8.8	8.0	8.3	10.2	11.0	9.8	10.3
59.0	76	7.6	8.3	7.1	7.7	8.6	10.0	9.2	10.0
				2. Clefts of Left Side					
46.0	8	5.4	6.2	5.5	5.4	7.5	6.5	7.4	7.0
48.0	11	7.9	8.0	7.2	7.3	9.4	9.0	9.2	9.0
50.9	59	7.4	8.3	7.1	6.8	9.1	8.4	8.9	8.6
51.2	34	7.5	8.1	7.0	7.3	9.1	8.5	8.3	9.3
51.4	42	7.5	8.8	7.0	6.8	9.3	8.2	9.0	8.5
53.6	71	8.0	8.6	7.2	7.5	9.4	8.8	8.8	8.9
54.0	20	7.6	8.0	7.4	6.8	9.6	8.2	9.2	8.6
55.3	63	8.3	7.8	7.1	7.3	8.5	9.7	9.0	9.6
56.5	49	8.0	9.2	7.8	7.6	9.5	9.3	9.6	9.8
56.7	47	8.3	8.5	7.4	8.0	9.0	10.2	9.3	9.5
56.8	56	7.9	8.0	7.5	7.7	9.3	9.2	9.2	8.6
56.9	21	8.3	9.1	8.2	7.8	10.1	9.4	9.8	9.7
57.8	89	7.8	8.4	7.2	7.2	9.4	8.6	8.8	9.2
57.8	78	7.9	8.0	7.2	7.2	9.5	8.5	9.0	9.2
58.7	64	8.5	9.0	7.5	7.5	9.6	8.8	9.0	9.0
58.9	81	7.6	8.2	7.1	7.0	9.2	8.5	9.0	8.5
59.7	95	8.5	9.1	8.4	7.9	10.1	9.2	9.5	9.5
60.1	74	9.0	9.9	8.2	8.0	10.1	9.9	9.6	9.6
61.7	240	8.8	9.6	8.3	8.4	....	....	9.5	10.2
63.4	190	8.5	9.2	8.0	7.5	10.3	9.0	10.0	9.3
66.1	186	8.6	9.5	8.4	7.8	10.3	9.5	9.5	9.5
66.4	278	9.5	9.1	8.3	8.6	10.0	10.1	10.0	9.8
67.2	225	8.6	9.0	8.4	8.2	10.0	10.0	10.0	9.8
67.6	218	10.0	10.3	9.5	9.0	11.2	10.4	10.6	10.7
70.5	380	9.5	10.0	9.0	8.7	11.0	10.5	10.5	10.0
75.1	391	10.0	10.9	9.4	9.3	11.4	11.0	10.7	11.0
				3. Clefts of Right Side					
50.0	10	8.4	7.8	6.9	7.4	8.7	9.6	8.1	9.1
50.9	13	7.1	7.2	6.3	6.6	8.3	8.7	8.4	8.6
51.6	16	8.4	8.0	7.3	7.6	9.0	9.5	8.5	9.2
51.7	77	8.8	8.5	7.5	8.1	9.0	9.5	8.9	9.6
52.0	48	8.5	7.0	7.0	6.8	8.5	10.2	9.0	9.3
52.2	41	9.3	8.5	7.5	8.0	9.5	10.0	9.5	9.3
53.6	40	8.8	8.1	7.5	8.3	9.0	9.6	9.2	9.7
56.2	50	9.7	8.7	8.1	8.3	9.6	10.2	10.1	9.8
56.9	121	9.1	7.7	7.5	7.4	9.1	9.0	8.9	9.2
57.0	71	9.4	8.9	8.1	8.1	9.7	10.4	9.6	9.7
57.2	97	8.7	8.4	7.3	8.0	9.4	10.0	9.0	9.7
57.6	76	9.4	8.6	8.5	8.6	10.0	10.5	10.3	10.0
58.5	48	10.0	9.0	8.2	8.5	10.5	11.0	10.0	10.4
59.2	101	8.9	8.0	7.4	8.0	9.1	9 9	9.1	9.8
59.5	111	7.9	8.4	8.0	7.8	9.8	9.9	9.7	9.8
60.5	148	9.0	8.2	9.0	8.2	9.2	10.6	9.4	9.8
63.7	232	8.8	8.8	7.2	8.0	8.9	10.0	9.2	10.0

TABLE 2.—*Comparison of Means and Coefficients of Regression*

Measurements		a	$y \pm \sigma_y$	Diff.±P.E.	R.	P.	$b \pm \sigma_b$	Diff.±P.E.	R.	P.
A. Normal Child										
Auriculolabial (midline), 89 cases	R	3.8575	9.5584±0.0828	−0.0023±0.1194	0.0193	0.98	0.0948±0.0070	−0.0004±0.0095	0.9916	0.32
	L	3.2944	9.5607±0.0860				0.1042±0.0063			
Auriculonasal (side), 91 cases	R	3.1869	8.3813±0.0757	0.0187±0.1099	0.1702	0.87	0.0867±0.0063	−0.0030±0.0093	0.3216	0.75
	L	2.9879	8.3626±0.0796				0.0897±0.0068			
Auriculonasal (midline), 91 cases	R	4.0433	9.8132±0.0820	0.0363±0.1141	0.3183	0.75	0.0963±0.0064	0.0029±0.0089	0.3255	0.75
	L	4.1803	9.7769±0.0792				0.0934±0.0061			
Auriculonasion, 88 cases	R	3.4479	9.7170±0.0912	0.0431±0.1288	0.3346	0.74	0.1046±0.0070	0.0033±0.0102	0.3267	0.74
	L	3.6056	9.6739±0.0910				0.1012±0.0075			
B. Maldeveloped Child										
1. Bilateral Clefts										
Auriculolabial, 14 cases	R	0.4309	7.7357±0.1350	0.1071±0.1846	0.5802	0.56	0.1355±0.0270	0.0489±0.0460	1.0752	0.29
	L	2.9609	7.6286±0.1258				0.0866±0.0366			
Auriculonasal (side)	R	1.2532	7.2857±0.1093	0.0357±0.1442	0.2476	0.81	0.1119±0.0209	0.0362±0.0313	1.1564	0.25
	L	3.1719	7.2500±0.0908				0.0756±0.0233			
Auriculonasal (midline)	R	1.3956	9.2286±0.1732	0.1857±0.2102	0.8834	0.38	0.1452±0.0442	0.0810±0.0581	1.3943	0.16
	L	5.5786	9.0429±0.1192				0.0642±0.0376			
Auriculonasion	R	1.0421	9.1500±0.1456	0.1929±0.1846	1.0450	0.30	0.1503±0.0272	0.0307±0.0339	0.9070	0.37
	L	2.5063	8.9571±0.1135				0.1196±0.0201			
2. Clefts of Left Side										
Auriculolabial, 25 cases	R	2.2171	8.5000±0.1837	0.5346±0.2577	2.0745	0.04	0.1120±0.0158	−0.0032±0.0211	0.1504	0.89
	L	1.4962	8.2654±0.1806				0.1152±0.0139			
Auriculonasal (side), 26 cases	R	1.8943	7.6385±0.1550	−0.1038±0.2274	0.4565	0.65	0.0977±0.0123	−0.0116±0.0170	−0.6810	0.50
	L	1.3187	7.7423±0.1664				0.1093±0.0117			
Auriculonasal (midline), 25 cases	R	2.9241	9.1760±0.1870	−0.5000±0.2481	2.0153	0.05	0.1066±0.0168	0.0074±0.0211	0.3495	0.73
	L	3.8576	9.6760±0.1631				0.0992±0.0128			
Auriculonasion, 26 cases	R	4.1375	9.3231±0.1526	−0.0384±0.2054	0.1870	0.85	0.0882±0.0144	0.0010±0.0180	0.0580	0.95
	L	4.2373	9.3615±0.1375				0.0872±0.0108			
3. Clefts of Right Side										
Auriculolabial, 17 cases	R	3.9703	8.2235±0.1328	−0.6118±0.2084	2.9360	....	0.0762±0.0312	0.0152±0.0522	0.2920	0.77
	L	5.4324	8.8353±0.1606				0.0610±0.0418			

Auriculonasal (side), 17 cases	R L	3.9068 2.5334	7.8647±0.1297 7.6059±0.1528	0.2588±0.2004	1.2914	0.19	0.0709±0.0311 0.0909±0.0354	−0.0200±0.0471	0.4250	0.67
Auriculonasal (midline)	R L	5.8552 5.5770	9.9176±0.1352 9.2529±0.1312	0.6647±0.1884	3.5281	....	0.0728±0.0325 0.0659±0.0323	0.0069±0.0458	0.1513	0.88
Auriculonasion, 17 cases	R L	5.1573 4.5342	9.5882±0.1003 9.2294±0.1416	0.3588±0.1736	2.0668	0.04	0.0794±0.0189 0.0842±0.0328	−0.0047±0.0379	0.1250	0.90
Normal Child with Pathologic Side of Maldeveloped										
Auriculolabial	N* P*	3.5800 2.3114	9.5596±0.0596 8.2488±0.1212	1.3108±0.1351	9.6990	....	0.0994±0.0047 0.1031±0.0127	−0.0037±0.0136	0.2689	0.78
Auriculonasal (side)	N P	3.0912 2.3565	8.3720±0.0549 7.7907±0.1133	0.5813±0.1259	4.6168	....	0.0882±0.0046 0.0946±0.0123	−0.0062±0.0131	0.4726	0.64
Auriculonasal (midline)	N P	4.1156 4.8840	9.7951±0.0570 9.7738±0.1129	0.0213±0.1265	0.1684	0.86	0.0948±0.0044 0.0850±0.0134	0.0098±0.0141	0.6905	0.49
Auriculonasion	N P	3.5305 5.0588	9.6955±0.0644 9.4512±0.0935	0.2443±0.1135	2.1524	0.03	0.1028±0.0051 0.0763±0.0104	0.0266±0.0116	2.2856	0.22
Normal Child with Normal Side of Maldeveloped										
Auriculolabial	N P	3.5800 3.2523	9.5596±0.0597 8.8140±0.1279	0.7456±0.1411	5.2825	....	0.0994±0.0047 0.0966±0.0155	0.0029±0.0162	0.1770	0.86
Auriculonasal (side)	N P	3.0912 2.3526	8.3720±0.0549 7.6256±0.1116	0.7464±0.1243	6.0032	....	0.0882±0.0046 0.0916±0.0123	−0.0034±0.0132	0.2579	0.79
Auriculonasal (midline)	N P	4.1156 3.8661	9.7951±0.0570 9.2071±0.1235	0.5880±0.1360	4.3239	....	0.0948±0.0044 0.0929±0.0147	0.0019±0.0154	0.1248	0.90
Auriculonasion	N P	3.5305 4.4297	9.6955±0.0644 9.2860±0.1083	0.4095±0.1260	3.2503	....	0.1028±0.0051 0.0843±0.0128	0.0185±0.0137	1.3465	0.18
Pathologic with Normal Side of Maldeveloped										
Auriculolabial	P N	2.3114 3.2523	8.2488±0.1213 8.8140±0.1279	−0.5652±0.1763	3.2066	....	0.1031±0.0127 0.0966±0.0155	0.0065±0.0201	0.3250	0.74
Auriculonasal (side)	P N	2.3565 2.3526	7.7907±0.1133 7.6256±0.1116	0.1651±0.1590	1.0383	0.30	0.0944±0.0123 0.0916±0.0123	0.0028±0.0174	0.1606	0.87
Auriculonasal (midline)	P N	4.8840 3.8661	9.7738±0.1129 9.2071±0.1235	0.5667±0.1673	3.3869	....	0.0850±0.0134 0.0929±0.0147	−0.0078±0.0199	0.3939	0.69
Auriculonasion	P N	5.0588 4.4297	9.4512±0.0935 9.2860±0.1083	0.1652±0.1430	1.1551	0.24	0.0763±0.0104 0.0843±0.0128	−0.0081±0.0165	0.4892	0.62

*N indicates normal and P, pathologic.

gestive of an actual difference due to shorter measurements on the left side. It is interesting to speculate that there may be some relation between short measurements on the left side and the predominance of clefts on that side.

The auriculolabial measurement is significantly shorter on the cleft side. This is to be expected, since the cleft is not in the midline. The difference is approximately 0.5 cm.

The auriculonasal (side) measurement in cases of unilateral cleft was not demonstrated to be significantly shorter on either side, but the average in cases of cleft on the right or left side was shorter on the noncleft side.

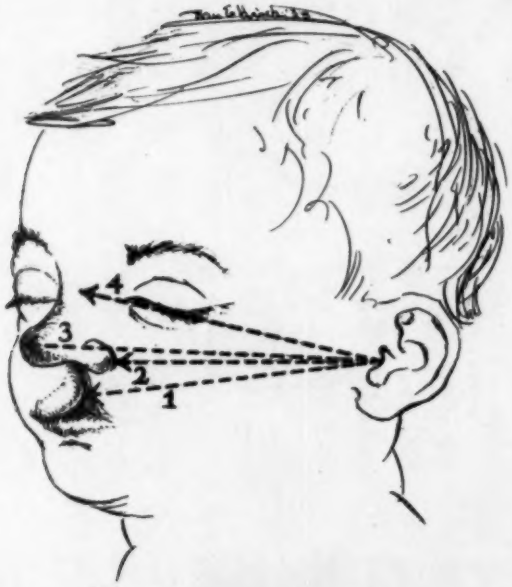

Diagram showing the measurements analyzed: *1*, the auriculolabial measurement; *2*, the auriculonasal (side) measurement; *3*, the auriculonasal (midline) measurement, and *4*, the auriculonasion measurement.

The auriculonasal (midline) measurement is significantly shorter on the noncleft side, demonstrating that the tip of the nose is shifted approximately 0.5 cm. toward the noncleft side.

The auriculonasion measurement in cases of unilateral cleft was not demonstrated to be significantly different, but in cases of cleft on the right or left side the average auriculonasion measurement was shorter on the noncleft side.

Considered as a whole, these findings suggest that the entire nose is slightly shifted to the noncleft side, the tip of the nose being shifted much more than any other part. Analysis of measurements for a larger

series of children would probably show significant differences in these dimensions where it is here indicated by the constant direction of differences.

COMMENT

The margin of error in the comparative measurements of the normal and cleft palate [1] must be negligible because the measurements were made on fixed tissues. The margin of error in the measurements of the face of the normal child and of the child with a cleft lip here presented are more variable because the measurements are made on movable tissues. Factors of muscle pull and personal interpretation enter more definitely into this study. The conclusions of the former study on the palate indicate that the tissues are all present but are out of contact. In this study there is in some instances a variance of from 2 to 4 mm. From a clinical standpoint of operative effort, measurement of from 2 to 4 mm., either in the deficiency of the tissue in the palate or in the width of a cleft, is a definite surgical problem. On the face, however, a difference of from 2 to 4 mm. between the normal and the abnormal face is of no moment, because of the movability of these tissues. The study of this material indicates that the deformity does not increase with growth. This is an important finding which must be checked, because if accepted or proved true it presents a proposition fundamental to surgical repair, viz., in a condition of apparent deficiency, the potentiality of future growth is inherent. Clinically, this proposition is widely supported, because, in the observation of a considerable number of cases in which repair of the deformities of the face has been neglected to later years, the tissues out of contact have grown with the body.

SUMMARY

The dimensions analyzed demonstrate no tendency for the deformity due to cleft of the lip to increase with growth, and rate of growth in the face of the child with cleft lip appears to be the same as that in the face of the normal child.

In the child with unilateral cleft of the lip the entire nose appears to be shifted toward the noncleft side, the tip of the nose being shifted approximately 0.5 cm., which is greater than the shift of any other part of the nose.

UNUSUAL CARTILAGINOUS TUMOR FORMATION OF THE SKELETON

ERNST FREUND, M.D.
VENICE, FLA.

The purpose of this article is to report a few cases of cartilaginous tumor of the skeleton, which represent in part unusual forms of otherwise well known conditions (enchondroma, single osteochondroma and multiple cartilaginous exostoses) and in part an apparently rare form of a multiple intra-articular tumor formation which, to my knowledge, has not yet been described in the literature. The case which will be reported last is one of a true intra-articular osteochondroma, which developed in more than one joint on the basis of a peculiar hyperplastic change of joint cartilage and which had to be differentiated from similar formations as they develop typically in persons with hypertrophic arthritis and from other conditions usually considered as neoplastic changes of the joint capsule, such as chondromatosis of the joints.

As is so common in cases of cartilaginous tumor formation of the skeleton, besides the cartilaginous component a considerable amount of bony tissue was present. One is justified in speaking of the growth as a cartilaginous tumor, despite the fact that in some instances the bony component is prevalent, mainly because the cartilaginous portion represents the real active element in the tumor, the cellular proliferation of which results in the increase in size. The bony tissue replaces the cartilage; its significance is therefore merely secondary.

REPORT OF CASES

CASE 1.—*Enchondroma of the femur.*

A man aged 55 complained of pain in the region of the right hip. He had had periodic attacks of pain in the upper part of the right femur for the past eight years, which gradually became worse and interfered with his work as a farmer. The hip joint had never been stiff, and he had only a moderate limp for one year. There was no fever or loss of weight.

Physical examination revealed a smooth enlargement of the upper third of the right femur of hard bony consistency, which was moderately tender in a few places. The surrounding soft parts and the overlying skin were normal. There was no swelling of the inguinal lymph nodes. The motion in the hip joint was free in all directions, except for external rotation, which was slightly restricted. The Wassermann reaction was negative. Examination of the blood gave essentially normal results: red blood cells, 4,660,000; white blood cells, 9,700, and hemoglobin content, 90 per cent.

From the Orthopedic Department of the State University of Iowa, Iowa City.

A roentgenogram of the upper third of the right femur showed considerable enlargement, with very irregular bony structure. The old cortical bone had been entirely removed, and the expansion of the bone extended to the periosteal surface, where on the outer side a small prominence of irregular and porotic bony structure had formed. The inner architecture of the lesion was that of extremely coarse trabeculation and calcification with areas which were almost cystlike in appearance. There were some transverse zones of rarefaction running through the enlarged area, most likely representing incomplete fracture lines. The pathologic changes gradually extended upward and downward into normal bony tissue with

Fig. 1 (case 1).—Enchondroma of the femur in a man aged 55.

erosion of the cortical bone from within and considerable apposition of periosteal bone on the medial side of the cortical bone. The entire lesser trochanter had become invaded. There was no swelling of the soft tissue. Marked calcification of the wall of the femoral artery was present.

Two possibilities had to be considered on the basis of the roentgenographic and the clinical picture: The lesion could be either inflammatory or neoplastic. From the roentgenographic standpoint a chronic osteomyelitic lesion could produce such a picture, although the clinical history, with the absence of more acute symptoms and fever and the beginning of clinical manifestations rather late in life, spoke primarily against it. The roentgenogram, also, on more careful

examination, showed a few features which did not fit well into the common picture of osteomyelitis. The localization in the upper third of the femur would be an unusual site for pyogenic osteomyelitis. The amount of periosteal bone production was insignificant and did not correspond to the marked degree of bone destruction, if the latter were due to an inflammatory process. On this basis, a diagnosis of pyogenic osteomyelitis could be ruled out from a clinical and a roentgenographic standpoint.

There was nothing to suggest a specific inflammatory lesion, such as syphilitic osteomyelitis. The Wassermann reaction was negative, and a gummatous lesion would also have produced more periosteal reaction than was present in this case.

Among the neoplastic lesions, several had to be considered. The almost cystlike appearance of the lesion, with the blowing up and thinning out of the cortex, could suggest a benign giant cell tumor. Against it were the age of the patient (giant cell tumor usually occurs toward the end of the second or in the third decade of life) and the localization of the tumor (giant cell tumor is of epiphysial origin and commonly situated in the lower end of the femur and not in the upper end). Still the possibility of an atypical giant cell tumor had to be kept in mind.

A diagnosis of osteogenic sarcoma could safely be ruled out because of the long duration of the lesion (at least eight years), although from the roentgenogram one could be reminded somewhat of the *forme géodique* of a central cystic diaphysial sarcoma.

Along the same line, Ewing's tumor could be mentioned as a diaphysial lesion, which in the chronic stage may resemble an inflammatory process, but there was no evidence clinically to substantiate such a diagnosis.

There remained one form of tumor which quite often is seated in the upper end of the diaphysis of the femur and which could explain the clinical as well as the roentgenographic picture. I mean the embryonal chondroma or enchondroma of the femur, which frequently is a silent tumor during the greater part of the patient's life, but at a later age it may show more marked proliferation of its cells and may even become a malignant chondroma. The irregular calcification, with areas which were almost cystlike in appearance, the erosion of the cortical bone from within and the relatively weak periosteal reaction were well compatible with the diagnosis of embryonal chondroma of the femur, with greater activity during the last eight years.

To arrive at a definite diagnosis, a biopsy was performed. The periosteum over the enlarged portion of the femur was smooth and thin. The cortical bone on the outside was thinned to about 1 mm., but it was in no place completely interrupted. The endosteal surface was eroded by a transparent gelatinous bluish white tissue, which was typical of embryonal chondroma or myxochondroma.

Histologically, the tumor tissue was characterized by starlike cells, with a loose, watery ground substance between the protoplasmic processes of the cells. The ground substance was slightly basophilic. In some areas the basophilia became more marked, and the cells assumed here more the spherical shape of cartilaginous cells. Owing to the interstitial growth of the tumor tissue with augmented intraosseous pressure, the bony tissue gradually disappeared as a result of osteoclastic resorption of bone. There was, however, everywhere a sharp borderline between the tumor and the bony tissue. The bone marrow formed a kind of fibrous capsule around the tumor tissue which imitated in many places a perichondrium. The configuration of the tumor toward the surrounding normal bone marrow was convex, corresponding to the pressure within the tumor tissue. The tumor became subdivided into many smaller lobules by stronger bony trabeculae. The convexity of the lobules was always turned toward the normal marrow spaces.

There was no infiltrative tumor growth, so that the haversian canals of the cortical bone were free from invasion by the tumor. Owing to continuous apposition of the periosteal bone, the cortical bone became gradually displaced toward the periphery, which, combined with the resorption of bone at the endosteal side, led, to the blowing up and thinning out of the cortical bone over the tumor. The roentgenographic diagnosis could thus be confirmed by biopsy.

In this case an enchondroma was being dealt with, which in many places still had the appearance of a myxoma, so that the classification as embryonal enchondroma seemed to be justified. There were no histologic signs of malignancy. The clinical history, with increasing pain and weakness of the leg, suggested, however, a more rapid growth within the last few years, so that the possibility of at least a mild local malignant growth had to be considered. Roentgen therapy was instituted. During two years' observation and frequent roentgenographic control examinations, no increase in the size of the lesion could be noted; it even seemed that there was a greater tendency to calcification. A long leg brace could gradually be discarded.

CASE 2.—*Osteochondroma ossis calcis.*

A woman aged 45 first noticed a growth on her left heel eighteen years before the present examination. It started gradually and then became larger; the skin over it hardened, but never broke down. The patient was operated on eight times, the first time about fourteen years before and the last time about three years before the present examination. The tumor had recurred since and was growing slowly all the time. Recently it had extended to the outside of the foot.

On physical examination the skin over the left heel was found scarred in many places and firmly adherent to the underlying structures. There was an irregular knobby growth on the os calcis, especially on its inferior and posterior aspects, apparently also involving the cuboid bone and the base of the fifth metatarsal bone. The tumor was firm and solidly attached to the bone. The skin over it was not discolored and not tender.

Roentgenograms showed an irregular configuration of the os calcis, which appeared enlarged, especially on its plantar surface, where an irregularly calcified dense outgrowth was present. The tumor was of a somewhat lobulated appearance and extended mainly along the plantar side of the os calcis in the form of a coarse network of bony trabeculae. There was also some spotted calcification in the plantar soft tissues close to the tumor. The calcaneocuboid joint was practically obliterated.

On the basis of these findings, the diagnosis of osteochondroma of the os calcis was made. Besides the location, the late onset of the growth was unusual (the patient was 27 years old when she first noticed the tumor). As a rule, clinical symptoms of osteochondroma start earlier in life; the active growth of the tumor seems to be intimately related to the process of enchondral ossification of the skeleton and comes commonly to a stop whenever the bone growth stops. It seems that the cartilaginous cover of the tumor is under the influence of the same stimuli as the cartilaginous epiphysial plate, which means that the tumor will show a tendency to grow according to the skeletal growth, but there will rarely be autonomous proliferation. It is rare to observe persistent growth of an osteochondroma after the twentieth year of life, and it is even less frequent to find the tumor developing after this period.

It is hard to assume that the tumor was present since childhood and enlarged after a latent period of so many years. Against such an assumption is the localization in such a highly sensitive region as the heel, in which the smallest tumor formation would readily be noticed. It cannot be entirely denied, of course, that the tumor germ was preformed around the os calcis. A certain fact, however, seems to be that the growth did not become manifest before the twenty-seventh year of life.

Another unusual feature is the frequent recurrence of the tumor, despite eight attempts at surgical removal. As a rule, one succeeds quite easily in the radical removal of a simple osteochondroma. There must have been some particular factor in this case which brought about the peculiar clinical course. First of all, one could be inclined to doubt the correctness of the clinical diagnosis—osteochondroma. To dispel such doubts, a biopsy was performed.

An irregular, nodular tumor was found consisting of cartilaginous and bony tissue and resembling a cauliflower in configuration. Although very irregular, the tumor was sharply outlined against the surrounding tissues, toward which it protruded with nodular cartilaginous formations.

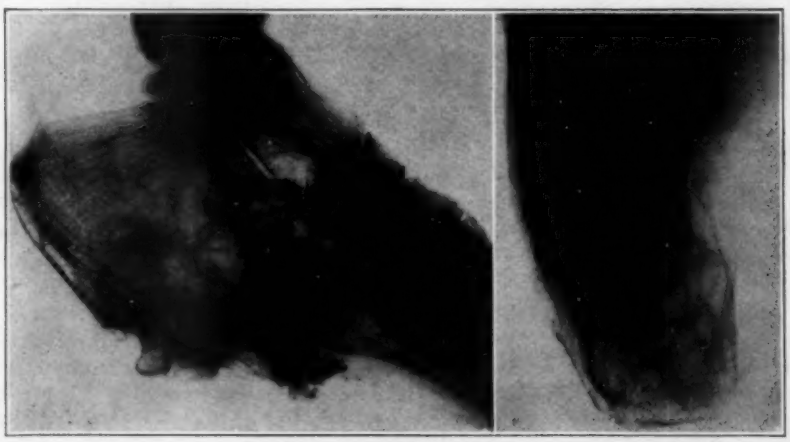

Fig. 2 (case 2).—Osteochondroma of the heel in a woman aged 45. The picture was made after the seventh recurrence of the tumor.

The microscopic examination confirmed the diagnosis of osteochondroma; most of the tissue removed consisted of mature hyaline cartilage well covered by a perichondrium-like dense layer of fibrous tissue. The deeper strata of the hyaline cartilage showed enchondral ossification with the formation of cellular columns and an irregular zone of provisory calcification. The rather porotic spongy bone resulting from this process of enchondral ossification was embedded in hyperemic fatty-fibrous bone marrow. There were no signs of malignancy.

In this case an osteochondroma was being dealt with which was unusual only so far as it showed many nodular cartilaginous prominences on the surface. A lobulated appearance of an osteochondroma is not infrequent; the resemblance to a cauliflower is, however, by no means typical. I think that the abnormal appearance of the tumor was due to the extremely unusual localization. The tight soft tissues on the plantar

side of the feet and the severe pressure effect exercised on this region with weight bearing must modify considerably the cartilaginous tumor growth and change it from a unicentric expansion to a pluricentric growth, depending on the space available and the counterpressure encountered. In adapting itself to the narrowness of the space, which presents itself to invasion, the tumor assumes first a multilobulated and finally a multinodular appearance. It may even be that some of the nodules become detached from the mother growth to form later independent centers of cartilaginous proliferation. (This would explain the roentgenographic presence of the calcified spots in the plantar soft tissues close to the tumor.)

The dispersed tumor particles, and the corrugated relief of the primary tumor make it understandable that radical removal will be difficult. The extension of the tumor permits complete removal only by radical resection of the heel; other less radical procedures are bound to fail from the start. The frequent recurrence in this case was by no means a sign of malignancy; it was due to nothing but inadequate surgical intervention. Every benign tumor, fibroma, lipoma, etc., is likely to recur if not removed entirely. The same is true of an osteochondroma, especially for its cartilaginous component, which represents the actively growing part of the tumor. One can stop the growth of a cartilaginous exostosis by removing the cartilaginous cap. The bony portion, although as a rule making up the greater part of the tumor, is merely the result of the proliferation of cartilage and its subsequent replacement by bone according to enchondral ossification.

It is possible that the localization of the tumor, inducing frequent traumatization by weight bearing and by the shoe, may have stimulated cellular proliferation and thus have rendered the surgical problem even more difficult. After eight failures to eradicate the tumor, the best procedure would be the amputation of the foot. This is preferred to the resection of the os calcis, which is too disabling an operation, and the possibilities of plastic repair are very poor.

CASE 3.—*Multiple cartilaginous exostoses with involvement of the joints.*

A man aged 23 stated that his condition started at the age of 19, when he fell from a horse, on the right side; gradually an enlargement of the right shoulder developed and reached the size of a baseball. It supposedly disappeared under chiropractic treatment. A little later, stiffness appeared in the right hip, with a slowly increasing limp. Also the spine became restricted in motion, and there was pain in the lumbar region and in the shoulders.

On physical examination the patient appeared shortly built (height 4 feet and 11 inches [150 cm.] and weight 112 pounds [50.8 Kg.]) with many palpable exostoses on most of the long bones of the skeleton. The upper extremities showed the characteristic disturbances of growth, with bowing of the radii and shortening of the ulnae. There was marked restriction of motion in both shoulder joints, especially of external rotation, which when tried was very painful.

The right hip joint appeared ankylosed in a position of 20 degrees of abduction, 15 degrees of flexion and 45 degrees of external rotation. A hard bony mass could be palpated in the inguinal region extending downward to the femur. It was very tender on palpation. Huge exostoses were present around the knee joint and on the lower end of the femur as well as on the upper end of the tibia.

The left lower extremity was more than 1 inch (2.5 cm.) shorter, but appeared longer because of the upward tilting of the right half of the pelvis (to compensate for the abduction of the right leg). The left hip joint was markedly restricted in motion, and there were only 45 degrees of flexion, 25 degrees of abduction and 20 degrees of external rotation. The upper end of the femur seemed to be enlarged in the same manner as the right femur.

The spine was without lateral deviation but showed marked rigidity in the sacrolumbar junction and pain on lateral motion.

Fig. 3 (case 3).—Multiple cartilaginous exostoses in a man aged 23. Note the bulbous enlargement of the metaphysis of the humerus with normal joint ends and the pedunculated exostoses of the ribs.

Roentgenograms were taken of all parts of the skeleton. They showed a picture of multiple cartilaginous exostoses, which was unusual because of the enormous enlargement of the metaphysial regions close to the shoulder and the hip joints.

The regions around both shoulders showed essentially the same change. The upper third of the humerus was enlarged and presented an irregular but smooth periosteal surface. There were several bony prominences on the enlarged portion of the humerus. The porotic spongy bone of these exostoses was in direct connection with the bony trabeculae of the diaphysis, which means that the exostoses belonged to the bony structure of the humerus and were not simply superimposed on the periosteal surface. The pronounced, almost diffuse enlargement of the

upper ends of the humerus with the porotic but coarse bony structure suggested that almost the entire upper third had been transformed to an "exostosis," replacing the metaphysis. The upper epiphyses were well developed, the joint surfaces were smooth and there was normal bony structure. On the left side the scar of the epiphysial plate was still visible.

The bones of the forearm showed the more common deformities, such as shortening of the ulnae and bowing of the radii, with exostoses of considerable size along the diaphyses.

Many of the upper ribs showed deformation of the posterior halves, owing to the presence of extensive, irregularly formed exostoses.

The neck of the femur showed tremendous enlargement by an irregular and porotic bony mass, which presented a smooth but uneven periosteal surface and did not extend into the capital and trochanteric epiphyses. The head of the right femur, however, was surrounded by irregular excrescences along its joint margins. The changes were by far more marked on the right side, the bony structure on the left being more dense and homogeneous.

There were other unusual changes in the pelvic bones and in the lumbar portion of the spine. The os pubis was markedly enlarged on both sides but had smooth surfaces. Its bony structure was cloudy and porotic. The configuration of the crest of the right ileum was also irregular where a continuous string of coarse but porotic bony excrescences was found. Both sacro-iliac joints appeared to be solidly fused, and from the upper corner of the right sacro-iliac junction a large densely calcified bony mass extended up to the third lumbar vertebra, firmly uniting these different skeletal portions with each other.

Considerable enlargement of the upper metaphysis of each fibula was also noticed. There were large exostoses at the ends of the femurs and upper ends of the tibias. These changes were less marked around the ankle joints.

To improve the motion in the right knee joint, an exostosis was removed from the upper end of the tibia. Subtrochanteric osteotomy was performed on the right femur to realine the leg. The patient insisted on a more extensive operation because of the pain and the disability in sitting and dressing. Therefore, the region of the right hip was exposed by a Smith-Petersen incision. The entire upper end of the femur and the adjacent portion of the ileum were the site of extensive proliferation of bone. The cortex was only of eggshell thickness, the bone marrow was red, and there was marked osteoporosis. To expose the head, it was necessary to chisel off huge masses of bone from the trochanter and the neck. The head of the femur appeared normal. The limitation of motion was due to the mechanical obstruction of the joint by the new bony mass. Enough bone was removed to obtain 25 degrees of abduction and 30 degrees of flexion.

This case, although definitely one of multiple cartilaginous exostoses, shows several features which are not typical. As a rule, patients with multiple cartilaginous exostoses become aware of the deformities in childhood and certainly before bone growth stops. In this case there was a relatively late onset of symptoms with increasing severity a long time after the full skeletal growth had been reached. Generally, multiple cartilaginous exostoses cease to grow around the twentieth year of life, when most of the epiphysial plates disappear. They may, of course, persist during the entire life, but clinical symptoms are rarely progressive, and the appearance of new exostoses after skeletal growth has ceased is extremely unusual.

Most of the symptoms of this case were due to the enlargement of the bones close to the big joints of the body, leading to restriction of motion and considerable pain. The pronounced participation of the great joints of the body (shoulder, hip and, to a lesser degree, knee joints) forms an unusual feature in cases of multiple cartilaginous exostoses. In most instances the exostoses form prominences on the diaphyses of the long tubular bones, pointing typically toward the middle of the diaphysis. The bones may become considerably deformed, but more extensive alteration in the motion of the joint does not belong to the typical clinical picture.

In this case the exostoses formed thinly pedunculated bony prominences only exceptionally. They rather involved the entire circumference

Fig. 4 (case 3).—Enormous enlargement of the metaphyses of both femurs with the heads of normal shape, but interference with motion of the hip joint by a periarticular bony obstacle; enlargement of the ossa pubis and a solid bony mass at the right lumbar region, uniting the lumbar portion of the spine with the pelvis.

of the affected bony portion, thus leading more to the picture of a diffuse hyperostosis than to that of cartilaginous exostoses. The closeness of the bony masses to the joints explains the restriction of motion, despite the fact that the ends of the joints or the epiphyses primarily do not participate in the pathologic process. It seems that the lesion is a purely extra-articular one, mainly metaphysial, and probably due to a disturbed formation of periosteal bone rather than to a lesion of the cartilage of the epiphysial plates. The cartilaginous cover of the metaphysis, which during the first years of life stays in direct continuity with the epiphysial

cartilage and the cartilage of the epiphysial plate, probably does not undergo the normal process of resorption; it may remain preserved to more considerable extent and may later lead, by its proliferation and enchondral ossification, to enlargement of the bony metaphysis, in the form either of a diffuse widening along the entire circumference or of a more typical exostosis, which, however, shows a rather wide bony pedicle.

Such rare cartilaginous exostoses seem to be considered in the literature as intra-articular localizations of the tumors. As I shall point out in the discussion of case 4, this is not correct. In the few cases reported in the literature in which multiple cartilaginous exostoses were complicated by participation of joints there was not a true intra-articular seat of the tumor, but, as in the case just presented, there was such marked enlargement of the juxta-epiphysial portions of the metaphyses that the joints became secondarily involved and the motion of the joints restricted.

The treatment in such cases is indicated by the degree of disability. The mechanical obstruction of the joints by the tumors has to be removed surgically. The operator, however, has to take into consideration the considerable osteoporosis and hyperemia of the tumors when he tries to reduce the bony obstacle.

CASE 4.—*Multiple intra-articular osteochondroma.*

A man aged 26 complained of tumors on the right ankle and knee and stated that as long as he could remember he had had a swelling on the outer side of the right knee and on the outer side of the right ankle. The right leg had grown faster than the left. The mass on the outer side of the ankle had become somewhat larger recently and caused some pain after walking. Changes in weather had no effect. Seven months before the present examination he had a semilunar cartilage removed from the right knee and had been without symptoms since.

Physical examination showed that the right lower extremity was 2 inches (5 cm.) longer than the left. The patient walked with a decided limp to the right, keeping the right leg in abduction. There was atrophy of the calf of 2½ inches (6.3 cm.). A bony hard tumor mass the size of a walnut, firmly connected to the tibia, could be palpated on the outer side of the right knee joint. There was no tenderness or sign of inflammation. There was a linear scar 6 cm. in length on the outer aspect (removal of semilunar cartilage). Marked grating and pain were noted on extreme flexion. The right ankle was in a varus position. On the outer side, a bony mass the size of half a baseball was present, which was tender to pressure and not movable. The tibio-astragaloid joint had only a few degrees of plantar flexion and dorsiflexion; the subastragaloid joints were stiff.

Roentgenograms of the right knee joint showed considerable deformity of the lateral portion; especially the lateral condyle of the tibia seemed to be deviated toward the joint cavity by a mass of spongy bone which formed a part of the bony epiphysis. The joint surface of the lateral condyle was uneven and showed a dishlike impression. The lateral condyle of the femur showed a corresponding deformity, but to a much lesser degree, which could probably be explained by its

secondary involvement. The outer condyle of the femur was much smaller than the inner. Owing to the marked enlargement of the lateral condyle of the tibia, it seemed that the upper end of the fibula was not normally developed. It remained shorter, and its apex was below the scar of the old epiphysial line, while it was considerably higher on the normal left side. The inner condyles were of normal shape. The anterior compartment of the joint, mainly the suprapatellar pouch, contained from eight to ten joint bodies varying in size from that of a pea to that of a large cherry. They were sharply outlined with irregular and not very dense calcification.

Roentgenograms of the region of the ankle revealed marked deformity of the tibio-astragaloid joint. The astragalus was enlarged by a bony growth on the outer and posterior portion. The growth consisted of coarse bony trabeculation

Fig. 5 (case 4).—Multiple intra-articular exostoses in a man aged 26. The anteroposterior and the lateral view of the right knee are shown. Enlargement of the lateral condyle of the tibia, atrophy of the lateral condyle of the femur and joint bodies in the anterior compartment of the knee joint are depicted.

and was connected with the body of the astragalus. Because of the tumor, the entire joint surface of the astragalus became widened, especially in its transverse diameter.

Similar changes had also taken place at the lower end of the tibia. Right above the bony overgrowth of the astragalus the lower end of the tibia showed corresponding enlargement with a bony prominence of relatively dense structure. This prominence surrounded the astragalus from the superior and outer side, forming almost an outer malleolus. The lower end of the fibula was also slightly enlarged and displaced backward, so that the malleolar mortice was practically formed by the lower end of the tibia alone. The inner part of the lower end of the tibia appeared normal. Marginal exostoses of considerable size could also be seen in Chopart's joint and in the anterior portion of the subastragaloid joint, on the scaphoid and the os calcis as well as on the astragalus.

Changes probably of the same nature were also present in both hip joints, being more marked on the left side. The head of the femur was misshaped, and the neck was very short. The bony structure of the inferior portion of the head was irregular, and the joint surface over this area was definitely eroded. The corresponding area of the acetabulum was similarly involved. The changes in the right hip joint occurred mainly in the lower part of the acetabulum, where a small exostosis had formed.

All the other joints of the body were roentgenographically normal.

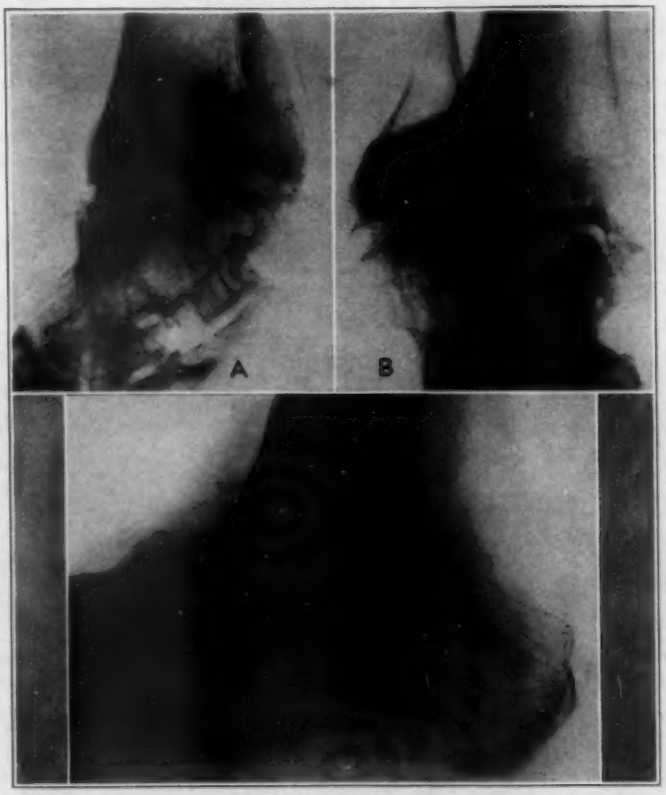

Fig. 6 (case 4).—*A* and *B*, lateral and anteroposterior views of the region of the right ankle. Enormous enlargement of the lateral sides of the tibia and astragalus by huge intra-articular exostoses (osteochondromas) are shown. *C*, lateral view of the region of the ankle after resection of the lower end of the tibia and astragalectomy.

The most striking features were the true lengthening of the right lower extremity for 2 inches and the involvement of several joints of the body (right knee, right ankle joints and left hip joint) by an intra-articular formation of exostoses. Despite the advanced changes in all of the affected joints, clinical symptoms of a marked degree were present only in the region of the ankle. The knee joint, from which the lateral semilunar cartilage had been removed seven months before the patient's admission to the hospital, showed normal

function despite extensive roentgenographic changes. There was not even a disalinement of the joint, although the outer condyle of the tibia was considerably enlarged. One would expect varus deformity of the knee if there were an enlarged outer condyle of the tibia and a normal one of the femur. But the (probably secondary) hypoplasia of the lateral condyle of the femur (maldevelopment due to pressure effect?) compensated well for the hypertrophy of the tibia, and there was no lateral deviation of the longitudinal axis of the joint, although the transverse axis was broken and run at different levels through the outer and the inner portion of the joint.

This apparently systemic disease of several joints of the body was of longer duration than in the other cases. The patient stated definitely that as long as he could remember the right lower extremity (which showed the main changes) grew faster than the left. There is no reason why the lengthening of 2 inches should not be attributed to the existing changes in the joint, which most likely stimulated the growth in length of the extremity at the site of the affected joint cartilages. I shall discuss this point more extensively later.

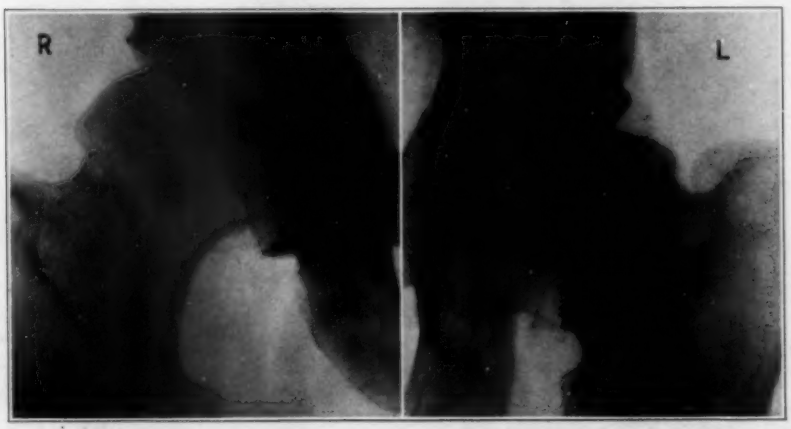

Fig. 7 (case 4).—Anteroposterior view of both hip joints. The short neck and irregularly shaped head of the left femur, especially in the inferior portion, are shown.

To liberate the patient from his chief complaint (stiffness and soreness of the right ankle), astragalectomy was performed. The involved anterolateral portion of the tibia and the lower end of the fibula were likewise removed. The foot was set back, the malleolar mortice was remodeled and the collateral ligaments were reconstructed by utilizing the tendons of the posterior tibial and peroneus brevis muscles, and firmly anchoring them in drill canals.

The patient made a good recovery. He was seen again sixteen months after the operation. The foot was in good alinement (fig. 6*C*). He was walking at least 4 miles every day; the foot never swelled but was sore after he had walked too much. There was still a lengthening of the right lower extremity of 1 inch (½ inch in the thigh and ½ inch in the leg). When both feet were on the ground, the right half of the pelvis was elevated 1 inch. There was slight left convex scoliosis of the dorsolumbar portion of the spine. There was a decided limp on walking, and the right calf was atrophied 3½ inches (8.9 cm.).

All the specimens removed surgically were studied histologically. A report summarizing the results of a careful study of twenty-six different large areas follows.

On gross inspection there was little similarity between the astragalus of the patient and a normal specimen. The astragalus was heavy and large (3 by 2 by 2 inches [7.6 by 5 by 5 cm.]). On the outer aspect of the body, where one would expect to find the articulating surface with the outer malleolus, there was a huge bony exostosis, which formed a continuous plane with the old joint surface of the body. There was, however, a definite borderline between the old joint surface and the cartilaginous cover of the exostosis. The joint surface of the astragalus was smoothly covered by yellowish white hyaline cartilage of a mature character; the tumor was covered by a rather thin and more primitive cartilaginous layer, which was bluish owing to the underlying hyperemic bone marrow shining through. Several smaller cartilaginous bodies, varying in size from that of a lentil to that of a pea, were noted on the surface of the huge exostosis. The large exostosis appeared definitely as a tumor formation. The smaller exostoses on the head of the astragalus and along the margins of the anterior lower joint surface were more typical of marginal exostoses, such as are frequently found in cases of hypertrophic arthritis. The joint cartilage, however, of the head and of the lower joint surfaces was well preserved. The posterior inferior joint surface appeared to be normal. Examination of the lower end of the tibia revealed a pathologic configuration, mainly due to the presence of a large exostosis at the anterolateral joint border. The osseous part of the tumor was formed by extremely dense spongy bone, with slightly hyperemic bone marrow. At the time of operation some small exostoses could also be observed along the margin of the posterior joint surface of the scaphoid.

On histologic examination the joint cartilage of the upper joint surface of the astragalus showed a normal appearance for the greater extent, with the exception that close to the lateral joint margin some degenerative changes were present, evidently due to mechanical irritation by the intra-articular osteochondroma. The tumor had clearly developed at the joint margin, where under normal conditions the end of the joint is covered only by a layer of synovial or primitive cartilaginous tissue. The tumor consisted of several lobules of irregular porotic and coarse bone tissue covered by a layer of cartilage. The latter had changed from primitive fibrous cartilage to mature hyaline cartilage, the change being dependent evidently on the different localization and the trauma.

At the lateral side, where only the joint capsule touched the cartilage cover of the exostosis, the cartilage was hyaline, with large cell groups in active proliferation surrounded by somewhat watery but basophilic ground substance. The more superficial layers were frequently covered by coagulated fibrin or were impregnated by a fibrinoid substance, as is the rule in soft tissues subjected to frequent mechanical traumatization. Those parts of the intra-articular osteochondroma which were in constant contact with the lower end of the tibia (which was changed essentially in the same way as the astragalus) revealed more pronounced structural changes in their cartilaginous cover. The different degree of pressure exercised on the relatively soft cartilaginous cover of the exostosis evidently accounted for these alterations. The cartilaginous layers were very irregular and showed all the characteristic signs of degeneration as they are encountered in fully developed degenerative (hypertrophic) arthritis. There were huge balls of proliferating cartilaginous cells glued together by hyaline ground substance, which underwent mucoid degeneration in many places. Tears and fissures coming from the surface often separated the cell groups from each other.

Entire tags or spherical portions of the cartilaginous cover could become worn off from the subchondral bone by mechanical friction. The bony tissue of the exostosis, as long as it was protected by cartilage, showed relative osteosclerosis in the subchondral zone. As soon as the protective cartilaginous layer disappeared, the pressure present within the joint cavity surpassed the physiologic degree which stimulates bone growth and developed into a bone-damaging factor, osteoclasia taking place. Below the degenerated cartilaginous cap there was increased resorption of bony tissue, with fibrous bone marrow and cystic formation. More in the periphery, where the pressure ceased, reenforcement of bony trabeculae was taking place by apposition of osteoblastic bone, an osteosclerotic wall of the cyst resulting. The fibrous bone marrow contained many irregular lacunar fragments of bony trabeculae. The entire picture corresponded exactly to the formation of subchondral cysts in cases of hypertrophic arthritis.

Where the cartilaginous layers of the lobules touched each other, there was degeneration of the cartilage of a type, which, to my knowledge, has never been observed in joints before. There was albuminoid degeneration with the appearance of dark blue granules in the cartilage. The cartilaginous cells remained intact and could be found surrounded completely by albuminoid granules. This typical form of degeneration of cartilage is common in the cartilages of the larynx or trachea, and also in the intervertebral disks, but it does not occur in the mature hyaline cartilage of the articulations.

The behavior of the joint cartilage where it bordered at or came in contact with the intra-articular exostosis was of great interest. In part, the joint cartilage was simply overlapped by the exostosis for about 2 cm., and in part the entire thickness of the joint cartilage had become perforated by marrow spaces. These marrow spaces, the result of enchondral ossification of the articular cartilage, brought about a communication between the bone marrow in the subchondral zone of the astragalus and the marrow spaces of the cancellous bone of the intra-articular osteochondroma. On the other hand, the remaining island of joint cartilage formed a good landmark, which showed how much the level of the joint surface had been displaced toward the joint cavity by the new growth. These pictures, as will be seen later, corresponded exactly to the common changes at the joint margins in cases of hypertrophic arthritis.

Where the exostosis overlapped the joint cartilage, a capillary space was to be seen between both cartilaginous layers for almost the entire length. This space made it easy to decide which was the old articular cartilage and which was the cartilaginous cover of the exostosis. The overlapping was mainly due to adaptation of the new growth to the narrowness of the space and to the existing intra-articular pressure. It could be expected that if there were damage to the cartilage by the overlapping, the soft and degenerated cartilage of the exostosis would cede first. As a matter of fact, the cartilaginous cover of the exostosis was very thin along the contact surface with the joint cartilage. It was necrotic in some places, the cells being preserved in the form of shadows, in other places the cartilage was evidently compressed with parallel arrangement of the cartilaginous cells, and in still other places the cartilage had entirely disappeared from the surface of the exostosis. In the latter areas, a secondary connection had taken place between the joint cartilage and the exostosis, with a layer of bony trabeculae lying almost continuously over the joint cartilage. The superficial layers of the joint cartilage took up lime salts wherever they came in contact with the newly formed bone; they remained uncalcified between the bony trabeculae. This

represented an excellent illustrative example of Erdheim's calcioprotective law, according to which only those portions of cartilage become calcified which are under static or mechanical stress.

The development of this amalgamation of tissues was probably as follows: The cartilaginous cover of the exostosis, suffering under increased pressure, disappeared completely and became substituted by fibrous tissue from the bone marrow. The fibrous tissue at a later stage of the process formed bony trabeculae along the surface to occlude the open marrow spaces. In some places it even seemed as though the two cartilaginous layers (joint cartilage and the cover of the exostosis) may have fused under pressure similar to the fusion of two metallic substances by heat.

The tissue connection between the exostosis and the joint cartilage may have become interrupted secondarily. A fissure was to be seen running through the

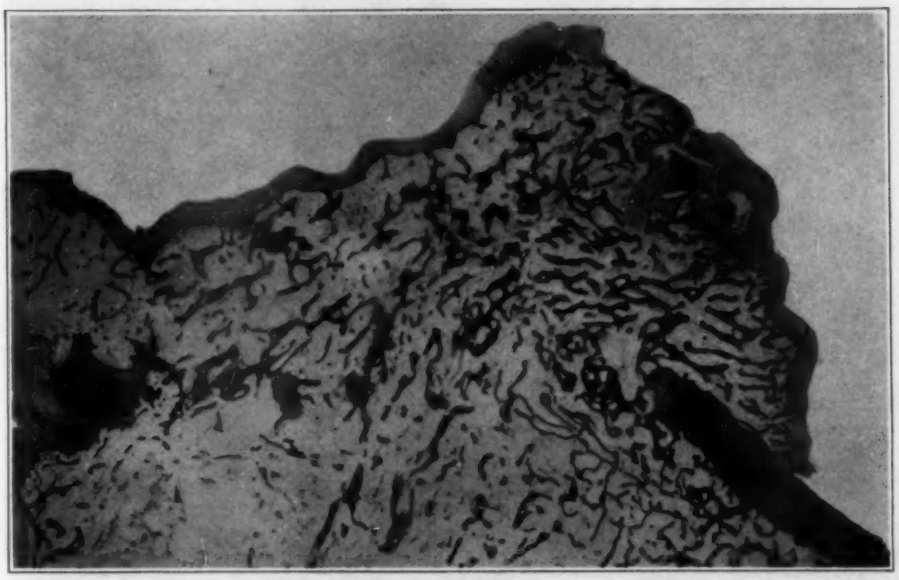

Fig. 8 (case 4).—Low power photomicrograph showing the large exostosis on the lateral side of the astragalus overlapping the joint surface. Several cartilaginous islands are included in the spongiosa, marking the previous level of the astragalus.

superficial layers of the joint cartilage, which had undergone mucoid degeneration. It was certain that some little motion must have occurred between the exostosis and the joint cartilage which was responsible for the localized tissue damaged with increased degeneration and the formation of the fissure.

Where the joint cartilage of the astragalus was overlapped by the exostosis, but only at these doubtlessly traumatized areas, degenerative changes of the old cartilage could be observed similar to the typical cartilage alteration in hypertrophic arthritis.

Close to the joint margin, the zone of provisory calcification enlarged considerably and was perforated in many places by hyperemic marrow spaces. Hand in hand with this increase in calcification of the joint cartilage went a slight

deviation of the cartilaginous-bony junction toward the joint cavity. This was a certain sign that more active enchondral ossification had been going on at the lower surface of the joint cartilage. The aforementioned cartilaginous islands were the remnants of joint cartilage which escaped enchondral ossification when the osteochondroma formed. They showed fully mature hyaline cartilage with many signs of proliferation and mucoid degeneration of the cell groups. They were surrounded on all sides by bony tissue and resembled more rests of the epiphysial plate than of joint cartilage.

The changes at the head of the astragalus and on its anterio-inferior joint surface were also of great interest. Here the process was not in such an advanced stage and permitted a better understanding of the earlier stages of this intra-articular tumor formation. It again was clear that the site of the pathologic

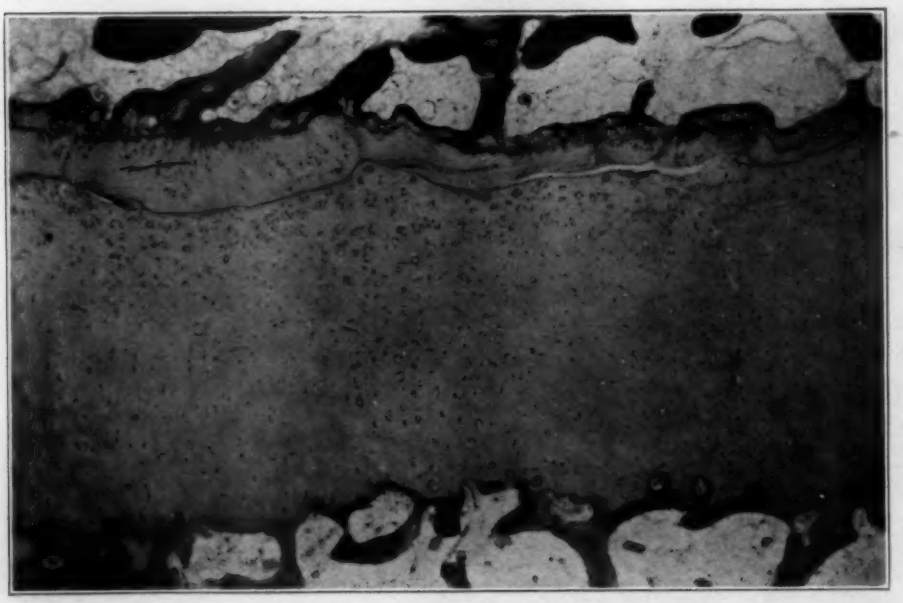

Fig. 9 (case 4).—Photomicrograph showing the joint cartilage of the astragalus, separated by a capillary space from the thinned out, partially necrotic cartilaginous cover of the intra-articular osteochondroma. Secondary changes in the joint cartilage (unevenness and accumulation of cells) due to pressure are seen.

process was at the joint margin. Where the joint surface of the head of the astragalus met the anterior joint surface of the subastragaloid joint, a nodular exostosis of the size of a pea was present. It consisted of a spongy bone the marrow spaces of which were in open communication with the cancellous bone of the astragalus. It had a cartilaginous cover which on one side was in direct connection with the articular cartilage of the antero-inferior joint surface of the astragalus and on the other side gradually disappeared toward the head of the astragalus. There remained only a layer of fibrous tissue. Whereas, the joint cartilage of the astragalus was perfectly normal, the cartilaginous cover of the

exostosis was of more primitive, small cellular and proliferative type, with many tears and fissures through the ground substance. The line of separation between these two different cartilaginous layers was rather sharp.

The lower surface of the cartilaginous cover of the small tumor nodules showed a number of marrow spaces, penetrating into the noncalcified cartilaginous layers, but altogether the process of enchondral ossification was not very active, and correspondingly there was a more or less continuous bony lamina separating bone marrow from cartilage (as is the rule whenever enchondral ossification becomes inactive). The bone marrow, even most superficially, was free from hematopoietic elements. This was different from exostoses with more marked growth activity, in which the marrow spaces close to the cartilaginous cover are always hyperemic and rich in cells.

The synovial membrane showed considerable proliferative changes, with many small calcified fragments included in the superficial layers. These inclusions did not impress one as primary bone formation in synovial tissue. They were

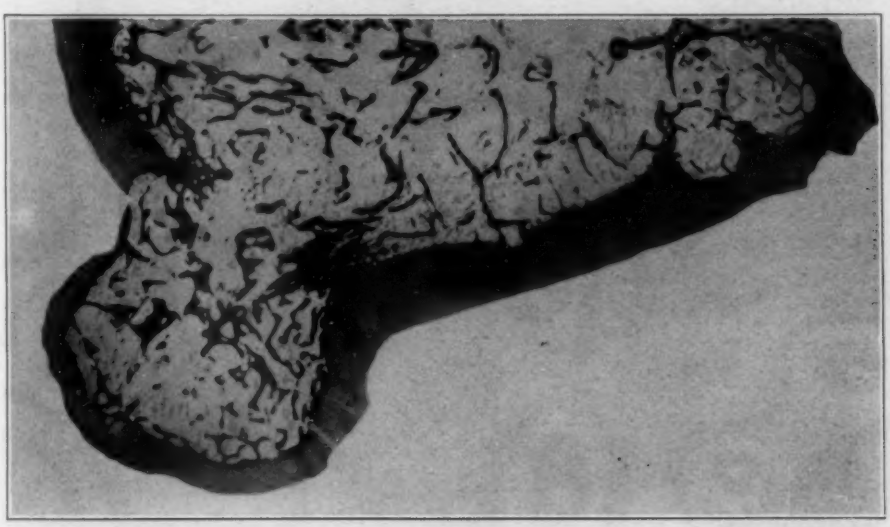

Fig. 10 (case 4).—Low power photomicrograph of the distal end of the astragalus. A pea-shaped exostosis between the head of the astragalus and the lower joint surface and small exostoses, not changing the level of the joint surface at the posterior border of the subastragaloid joint, are shown.

most likely small bony particles resorbed from the synovial fluid in which they had been floating after becoming loose from the surface of the intra-articular tumors.

A lesser degree of development than was shown by the osteochondroma on the head of the astragalus was represented by the changes at the posterior border of the subastragaloid joint, where a true exostosis in the sense of a bony prominence at the margin of the joint had not yet appeared. It was very clear from this picture that the intra-articular tumor formation started primarily with the invasion of joint cartilage by marrow spaces from below. At this site, however, the new marrow spaces occupied only the site of joint cartilage; they had not yet expanded to such a degree that the joint level had become altered.

This means that the joint cartilage had become only thinned out from below and replaced in part by bone marrow and spongy bone according to the process of enchondral ossification. But at present there were no signs of a still active enchondral ossification; especially, the zone of proliferation of cartilaginous cells was completely absent. One gained, therefore, the impression that the formation of exostoses came to a standstill relatively soon at the distal portion of the astragalus, whereas exostoses continued to grow at its superior and lateral margins and at the lower end of the tibia.

If one tries to subordinate the changes just described to the better known diseases of the joints, one meets with considerable difficulty. From the histologic point of view, the intra-articular tumor formation

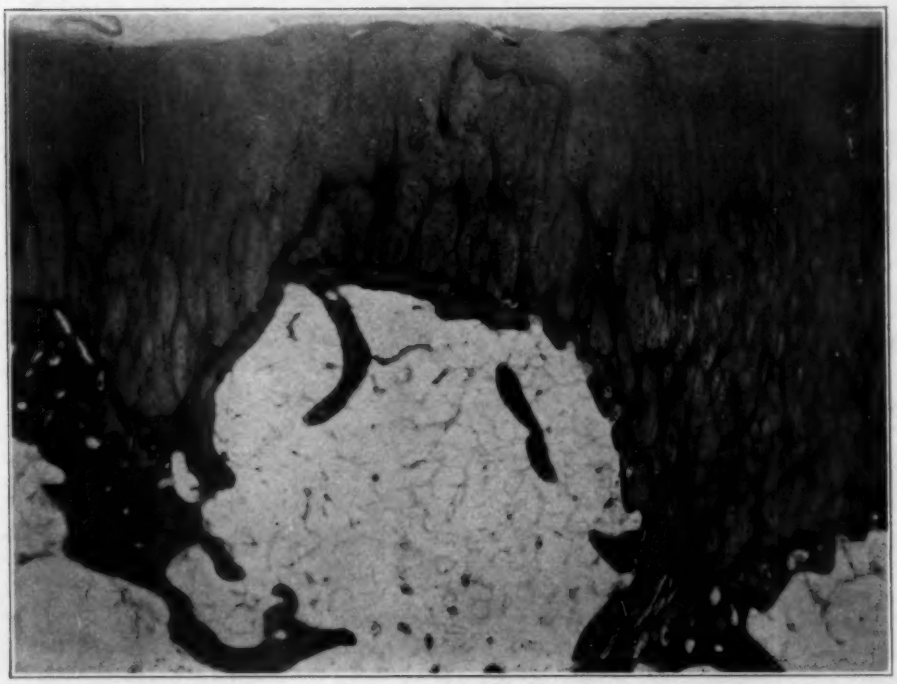

Fig. 11. (case 4).—Medium power photomicrograph of one of the exostoses at the posterior joint border. There are no signs of active enchondral ossification. Slight degenerative changes are seen in the joint cartilage over the exostosis.

had been classified as cartilaginous exostosis or osteochondroma, and there were a number of features in common with hypertrophic arthritis.

The marginal exostoses (frequently, but erroneously called osteophytes) are typical in cases of hypertrophic arthritis. Since Pommer's careful anatomic investigations, it is known that the exostoses in most instances owe their origin to the enchondral ossification of the marginal portions of the joint cartilage, which previously, owing to physiologic wear, trauma, infection, etc., has lost its normal elasticity. The sub-

chondral bone marrow, less protected by the degenerated cartilage, reacts to the increased mechanical irritation with an invasion of the joint cartilage by vessel spaces and vascular and cellular resorption. The resorbed cartilaginous portions are then replaced by bony tissue. This means recuperation of enchondral ossification, which has been quiescent since youth. For some not definitely established reasons (most likely because of the more marked tension stresses within the marginal portions of the articular cartilage), the peripheral parts of the articular cartilages show this "rejuvenescence" of the joint cartilage in the clearest form,

Fig. 12 (case 4).—High power photomicrograph of the border zone between the normal joint cartilage of the subastragaloid joint and the cartilaginous cover to the exostosis. The latter shows many small cartilaginous cells with little tendency to group formation. There are superficial layers with fibrillation and radial fissures, and small cartilaginous nodules in the subchondral bony lamina after herniation of noncalcified joint cartilage through a place of interruption in the zone of provisory calcification and subchondral bony laminae.

with the development occasionally of tumor-like marginal exostoses, resulting from the active process of enchondral ossification. The reactivation of enchondral ossification is the principal cause of the hypertrophy of the ends of the joint in cases of degenerative arthritis.

I do not think that this case is one of hypertrophic arthritis, despite the presence of some of the histologic characteristics of that condition. According to Pommer's functional theory of arthritis deformans, it is the lack of elasticity in the joint cartilage which starts the reactive changes from the side of the bone marrow. The morphologic manifestation of the lack of elasticity is given by degeneration of cartilaginous cells and ground substance. Fibrillation of the superficial cartilaginous layers, fissuring and greater tears can be observed in the noncalcified cartilage together with secondary proliferative cell activity. In case 4 such pictures along the free joint surfaces were absent entirely; on the contrary, the joint cartilage appeared perfectly normal, with the exception of the most marginal portions, where the structural alteration was certainly secondary, owing to the traumatization from the side of the intra-articular tumor. One cannot, therefore, attribute the extensive formation of marginal exostoses in this case simply to hypertrophic arthritis, even to a precocious or juvenile form.

The complete absence of one of the more common causative factors, especially trauma, and the unusually large size of the exostoses on the astragalus and tibia, apart from the histologic picture and the juvenility of the patient, were strong factors against a diagnosis of hypertrophic arthritis. Furthermore, the involvement of the knee joint with participation only of the lateral half of the articulation but without deviation of the longitudinal axis (no primary genu valgum) safely ruled out such a diagnosis.

The term intra-articular osteochondroma could easily induce one to think of the so-called osteochondromatosis of the joints, that peculiar hyperplastic metaplasia of the synovial membrane which may lead to an enormous amount of free and capsular joint bodies. Often in such cases the margins of the joints, with their synovial cover, are especially active sites of the formation of joint bodies. Osteochondromatosis, or better chondromatosis of the joints, however, most commonly affects only one joint and rarely two; in case two joints are found to be affected, they are usually symmetrical, both knee joints for instance. In case 4 there were several joints involved without any symmetry. Moreover, from an anatomic standpoint, there was nothing to suggest primary involvement of the synovial membrane. It did not show any specific alteration at the time of operation, and the histologic picture revealed only nonspecific hyperplasia with secondary inclusions of calcified material, but there was no metaplastic cartilage formation, as it is typical for chondromatosis. The presence of a greater number of joint bodies in the knee joint can well be explained by the breaking-off of parts of the intra-articular tumor. I have seen this process of separation of cartilaginous tags in the first stages of the tumor of the astragalus, and it is more than

likely that some of the smaller of these free cartilaginous cell groups may survive in the sufficient nutritive medium of synovial fluid and may even proliferate and calcify, thus leading to the typical picture of free joint bodies.

The best diagnostic assumption in this case is probably that of multiple intra-articular osteochondromas developing on a congenital basis, owing to an error of differentiation at those critical zones of the articulations where cartilaginous and connective tissues meet. All the exostoses had formed right at the joint margins and apparently only in small part on the expanses of the articular cartilage. It seems that the area of transition from cartilaginous to synovial tissue possesses more marked proliferative power than any other portion of the joints. (Some authors [Weichselbaum, Lubosch and others] have even expressed the belief that during the greater part of life the joint cartilage compensates for the daily wear by proliferation of cartilaginous cells at the margins.)

On the basis of such an assumption, the case is considered in relation to the multiple osteochondromas, as they also occur on a congenital (and strictly hereditary) basis. There is, however, a striking difference. In the case reported the seat of the tumor formation was purely intra-articular (the shafts of the bones were perfectly normal); there was an increase in length of the more affected extremity, and there was an increase in the size of the exostoses after skeletal growth had ceased. As a rule, multiple cartilaginous exostoses develop outside of the joint, most likely in connection with the cartilaginous cover of the metaphyses close to the epiphysial plates. (Not all authors agree on the periosteal origin of multiple cartilaginous exostoses, although there seems to be sufficient evidence that in a number of cases cartilaginous islands within the periosteum rather than the cartilage of the epiphysial plates are the primary site of the formation of cartilaginous exostoses.) It is quite conceivable that cartilaginous tumors in earlier life may form at any place around the epiphysis, especially at those cartilaginous parts of the epiphysial cap which later disappear, their place being taken by connective tissue of synovia and periosteum. It would seem that this area (similar to the zones of epithelial transitions, which according to Ribbert are predisposed to the formation of carcinoma) should be inclined to all kinds of errors of differentiation, and one should almost marvel at the rareness of such an occurrence rather than at its existence.

I would say, therefore, that in this case a congenital lesion in the development of joints, a hyperactivity of enchondral ossification at the joint margins, resulting in the formation of marginal exostoses was being dealt with. But a simple error of differentiation at the joint margins does not seem to be sufficient to explain the increase in length

of the right lower extremity and the peculiar deformity of the entire lateral condyle of the tibia. There must be something more than an error of differentiation at the joint margins to clear up the diagnosis.

It is impossible to make the exostoses at joint margins alone responsible for the increased length of the extremity. The right lower extremity remained 1 inch longer even after resection of the lower end of the tibia and after removal of the astragalus. One has to look for a more general cause which could explain the development of the exostoses together with the increase in length. The only possible way to explain both facts is to assume that there was hyperactivity of enchondral ossification around certain joints during the period of physiologic growth in length.

The peculiar picture of the cartilaginous-bony junction at the lower surface of the articular cartilages is nothing but a petrified, extinct process of enchondral ossification. The latter takes place not only at the diaphysial side of the epiphysial plates but also, to a much lesser degree, at the lower surface of the joint cartilages. Here *de potentia* enchondral ossification remains preserved throughout life, whereas at the epiphysial line it is definitely deprived of any further changes to reactivation as soon as the cartilage plate disappears. At the joint cartilages, enchondral ossification may become manifest again under pathologic conditions, for instance in hypertrophic arthritis or, even more, in tabetic arthropathy. This justifies the term "rejuvescence of joint cartilage" in such conditions.

The value of enchondral ossification of the articular cartilages for the growth of the length of the extremity has been denied by some authors. They have expressed the belief that all the increase in the length of the extremity takes place at the site of the epiphysial plates. However, as enchondral ossification takes place practically only at the diaphysial side of the epiphysial line, it is logical to assume that the bony epiphysis must enlarge by enchondral ossification of the joint cartilage. This means that the lower surface of the joint cartilage is of the same importance for the growth of the epiphysis as the diaphysial side of the epiphysial plate is for the growth of the length of the diaphysis.

One has to figure on a more general disturbance of the enchondral ossification of the joint cartilages than has found its histologic expression in form of the smaller and larger marginal exostoses on the removed specimens. The true lengthening of the right lower extremity for 2 inches suggests more diffuse activity of enchondral ossification, which, if involving the ends of the joint evenly, will, without affecting their shape, lead to an increase in the length of the individual bone and also of the extremity. I am unable to explain why only a relatively small number of joints are affected and why they are affected in an asymmetrical way if the main factor which influences enchondral ossification

is a central one, and it certainly is. Aside from the vague statement of a local predisposition of certain joints, I must admit that the etiology of this peculiar lesion of the joint remains obscure. However, I think that the pathogenesis could be cleared up quite well.

Once the final shape of the ends of the joints was obtained in this last case (around the twentieth year of life), the proliferative activity at the joint margins quieted down with the enchondral ossification, and the small exostoses (in the left hip and right subastragaloid joints) which had developed during the hyperplastic period did not increase in size later. (Histologically, the smaller exostoses were without growth activity; their cartilaginous cover was separated from the bone marrow by an almost continuous bony lamella.) This is another important analogy between the case of intra-articular cartilaginous exostoses reported here and the common cases of multiple osteochondroma. In both instances the exostoses do not represent true tumor formations; they signify merely hyperplastic changes of cartilage. They do not show an unlimited power of proliferation such as one would expect from a true tumor (blastomas); on the contrary, they cease to grow as soon as the skeleton has reached its definite shape, and they may even show regressive changes later in life.

The exostoses in the tibio-astragaloid joint and the enlarged lateral condyle of the tibia, however, do not fit into the category of simple hyperplastic formations. They are real tumors, with active and autonomous growth of their cartilaginous cover. The marked activity of growth is interfered with only by the limited space on the joint cavity. If left unhindered, it is likely that the osteochondroma at the joint margin of the astragalus would assume a similar pedunculated form, such as it often shows in the metaphysial region. Within the joint cavity, surrounded by a tight, nonelastic joint capsule, the tumor has to adapt itself to the narrowness of space, which explains the extensive overlapping of the joint surface.

In summary, I can say that on the basis of a hyperactive enchondral ossification of joint cartilage, true lengthening of an extremity occurred and marginal exostoses developed as simple hyperplastic formations. In a few places, the hyperplastic process went further, to true tumor formation, resulting in huge intra-articular osteochondromas.

The treatment can be symptomatic only as long as nothing is known about the cause of this peculiar disturbance of ossification. In the case reported, the removal of the tumors from the ankle joint by means of astragalectomy was satisfactory. The longer extremity was shortened for 1 inch, and a stable extremity was secured, permitting considerable motion without pain.

A REVIEW OF UROLOGIC SURGERY

ALBERT J. SCHOLL, M.D.
LOS ANGELES

FRANK HINMAN, M.D.
SAN FRANCISCO

ALEXANDER VON LICHTENBERG, M.D.
BERLIN, GERMANY

ALEXANDER B. HEPLER, M.D.
SEATTLE

ROBERT GUTIERREZ, M.D.
NEW YORK

GERSHOM J. THOMPSON, M.D.
ROCHESTER, MINN.

JAMES T. PRIESTLEY, M.D.
ROCHESTER, MINN.
AND
VINCENT J. O'CONOR, M.D.
CHICAGO

KIDNEY

Anomalies.—Baker and Colston[1] stated that clinically there is a definite syndrome of symptoms associated with horseshoe kidney. Various indefinite types of abdominal pain may be present, and particularly gastro-intestinal symptoms of varying degree, which are probably correctly attributed to the pressure of the isthmus of the horseshoe kidney on the rich plexuses of splanchnic nerves. The intimate relationship of these nerves to the underlying large vessels makes them particularly vulnerable to pressure exerted from the isthmus. Fusion of the lower poles of the kidneys is the more common type in this anomaly. In a series of 69 reported cases, fusion of the upper pole was found in only 1 case. The anomaly of horseshoe kidney may exist for years without symptoms, and many times it is encountered at necropsy without any clinical record of renal disease in the patient's past history. From a clinical standpoint, the symptoms are usually those of the disease which is present in one or both of the fused kidneys as a result of

1. Baker, W. W., and Colston, J. A. C.: Surgical Treatment of Horseshoe Kidney with Special Reference to Division of the Isthmus, J. Urol. **35**:264-285 (March) 1936.

the anomaly. The diagnosis of the condition is made as a result of investigation which may be undertaken to make a correct diagnosis of the condition of each kidney.

Plastic operation on the ureteropelvic junction of horseshoe kidney, pyelotomy for stones and nephrectomy for tumor, tuberculosis and pyonephrosis have been reported. Foley reported 5 cases in which division or resection of the isthmus of a horseshoe kidney was performed. Symphysiotomy, or division of the isthmus, has been reported in the literature in 24 cases. Seventeen of these were from European clinics. Baker and Colston reported 2 cases in which symphysiotomy was performed. The operative exposure in their cases was through an oblique lumbar incision, which was lengthened anteriorly for a greater distance than in the usual operation on the kidney. Dissection was carried down through muscles and transversalis fascia to Gerota's fascia. Before this structure was opened, it was freed posteriorly to the vertebral bodies, laterally and above as far as the diaphragm. Gerota's fascia was then opened at the level of the posterior lip of the renal sinus, and the perirenal vestments and Gerota's fascia were freed from the kidney by blunt dissection and carried toward the midline. The kidney and its vascular pedicle were thus cleanly and easily exposed. The reflected perirenal fasciae were retracted toward the midline, acting as protection to the peritoneum, and as they were left intact in a single sheath, they were utilized to close the renal fossa after the operative procedure. Exposure of the lower pole and isthmus is the most difficult part of the operation. The small vessels should be ligated and divided, but before any vessel of considerable size is divided, circulation in it should be interrupted for several minutes, and the portion of the kidney which it supplies should be observed to determine the amount of injury to the kidney which would be done by its ligation. After the isthmus has been satisfactorily exposed, in most cases a slight depression and thinning of the tissue will be noted. In some cases the point of union will be found to consist mainly of fibrous tissue with a small amount of renal parenchyma. When the line of division was chosen, the use of a right-angled stomach clamp facilitated exposure and compressed the tissue in such a way as to afford hemostasis while mattress sutures of chromic catgut were being applied. After the sutures were inserted through the kidney on each side of the isthmus, and fat or muscle was applied beneath the stitches to prevent cutting of renal tissue and to facilitate hemostasis, the isthmus was divided by the electrocautery. When the isthmus was satisfactorily divided, bleeding controlled and the right angle clamp removed, the kidneys were allowed to retract. In some cases a second mattress stitch placed through the ends of each stump, with fat and muscle over the raw tissue, may

be advisable. The relation of the pelvis and ureter may then be studied. If a stone is present, the kidney is then so freely mobilized that pyelotomy can be conveniently carried out; or if some indication is present for a plastic operation on the ureteropelvic juncture, or on the pelvis itself, it can be done with the kidney in a more normal position. At this stage it will usually be found that the course of the ureter is not straight, and it is for this reason that nephropexy is an important step in order to insure unobstructed drainage of the pelvis. The kidney should be placed as high as possible in the renal fossa with the lower pole rotated outward. This is best accomplished by two mattress stitches, the first of which is placed opposite the pelvis and carried through the capsule of the kidney, to be brought out above the twelfth rib, and the second of which is placed similarly beneath the true capsule at the lower pole, to be brought out to the lumbar muscles in such a way as to insure lateral axial deflection of the lower calices. Adequate drainage to both stumps should be instituted, and closure of the renal fossa by suture of Gerota's fascia to the quadratus lumborum and sacrospinalis muscles gives reenforcement to the nephropexy.

Gutierrez [2] stated that congenital anomalies are more commonly observed in the urinary tract than in any other system of the body and that fully 40 per cent of all pathologic conditions of the kidneys and ureters are due to malformations. The introduction of modern methods of urologic examination, and especially of pyelography and intravenous urography, has made it possible to diagnose preoperatively innumerable common malformations of this tract, the existence of which was formerly discovered only at operation or necropsy.

The various types of anomalies of the upper part of the urinary tract have been carefully classified anatomically and clinicopathologically in three tables, where they are systematized according to whether they concern the number, size, form and position of the kidney proper, its excretory apparatus or its blood and lymphatic supply.

The part played by these anomalies is by no means confined to diseases of the urinary tract alone. It is obvious that ectopia of the kidneys or ureters, abnormalities of contour, size or number, fusions, false openings of ureters and anomalous position of renal blood vessels or lymphatics may work havoc not only within the urinary system but also at points remote from the kidneys and ureters, giving rise to obscure abdominal or pelvic symptoms that are readily suggestive of lesions of organs within the gastro-intestinal or genital tract. These symptoms, which may even be wholly silent as regards the urinary tract, or in which urinary symptoms are only of a minor nature, are to

2. Gutierrez, Robert: Rôle of Anomalies of Kidney and Ureter in Causation of Surgical Conditions, J. A. M. A. **106**:183-189 (Jan. 18) 1936.

be attributed for the most part to pressure or traction exerted on other organs or nerve plexuses by the abnormal kidney or ureter. Often the patient has been subjected to one or more abdominal operations without relief before he is referred to the urologist. It is therefore of great importance in every case in which the slightest urinary symptoms have become manifest that a careful cystoscopic and urographic study be made, for experience has shown that such a study often reveals a congenital abnormality of the kidney or ureter as the underlying cause of the entire syndrome. In some cases of hypoplastic or aplastic kidney there may be an entire absence of urinary symptoms and a history of bilateral abdominal pain, or there may be lumbar pain and symptoms of chronic nephritis. Even in cases of hydronephrosis, symptoms of gastro-intestinal disturbance may predominate, or tumor formation may be the only symptom. In other cases there may be only slight frequency or dysuria, while in still others there may be severe renal colic and vesical tenesmus, accompanied by chronic cystitis or pyelitis.

It has been demonstrated that any such congenital anomaly is likely eventually to require surgical intervention, since it predisposes to poor function and to urinary stasis, with resultant retention and possible infection. In many cases of chronic pyuria and recurrent attacks of pyelitis or nephritis in children, the underlying cause has been found to be a malformation of the upper part of the urinary tract. Deficient function, nephritis and pyelonephritis, as well as hydronephrosis and calculus, are common in kidneys that are congenitally abnormal; and in cases in which only one kidney reveals an anomaly, the opposite kidney, although normally developed, may suffer from the additional strain imposed on it. Fused kidneys of various type, and especially horseshoe kidneys, are usually associated with some degree of ectopia and with abnormalities in the renal pelvis and in the form or number of the ureters. Hence they are frequently the site of pathologic lesions.

One of the most characteristic clinical syndromes is that which is associated with horseshoe kidney, in which there are always anomalies of the pelves, ureters and blood vessels. The three main clinical features of this syndrome are: (1) abdominal pain in the epigastric or umbilical region, (2) a history of chronic constipation with or without gastro-intestinal disorders and (3) urinary disturbances with early signs of chronic nephritis. Since frequently in the early stages the abdominal symptoms may predominate, a considerable period of time may elapse before the patient comes to the urologist. The abdominal symptoms are due to the fixation of the horseshoe kidney and the abnormal pressure it causes on the surrounding organs, nerves and blood vessels. The urinary symptoms are due fundamentally to lack of renal drainage,

with resulting infection and inflammation, all of which are directly traceable to the presence of the major renal anomaly.

Gutierrez placed special emphasis on the importance of a complete urologic and urographic examination in every case in which there are obscure and abdominal symptoms associated with minor urinary disturbances. Thus, cystoscopy will reveal any anomalous position of the ureteral orifices or of the trigon. A red and congested vesical mucosa may be a result of the urinary stasis characteristic of horseshoe kidney or of anomalies of the ureter or pelvis. Catheterization is an important means of revealing obstruction or ectopia of the ureters, which is so often associated with similar anomalies of the kidneys. Pyelography remains the method on which the chief dependence must be placed for correct diagnosis of anomalies of the urinary tract. Absence of a kidney or the aplasia, hypoplasia or hyperplasia of the renal organ may be shown by the method of intravenous pyelography, in some cases associated with cystoscopy, ureteral catheterization and retrograde or ascending pyelography to obtain the proper diagnosis. In the diagnosis of renal and ureteral anomalies, it is, of course, necessary always to secure a bilateral pyelogram.

Thomas and Barton [3] stated that an ectopic kidney is congenitally displaced and has never occupied a normal position in the body. An ectopic pelvic kidney is fixed within the bony pelvis or across the spine and derives its supply of blood from the adjoining large vessels and the iliac arteries. This anomaly is a defect of embryologic development and occurs before the eighth week. The incidence of congenital ectopic kidney is 1 in 822 necropsies and 1 in 547 urologic examinations. In both sexes, ectopic pelvic kidney must be considered when a tumor of the pelvis is found and when abortion occurs or when a normal pregnancy is interfered with by some mass in the abdomen or pelvis. Diagnosis requires cystoscopy, ureteral catheterization and bilateral pyelo-ureterograms. Congenital ectopic pelvic kidney may be symptomless. Treatment consists of nephrectomy if the symptoms are produced by the ectopic kidney, provided the contralateral kidney is normal. The extraperitoneal approach is satisfactory and safe. If no symptoms are produced, if drainage is good and if no infection is present, nephrectomy is not indicated.

Ptosis.—Woodruff and Scherer [4] described their operation for ptosis of the kidney as follows: The incision is made through the skin and subcutaneous fat and exposes the latissimus dorsi muscle, which is

3. Thomas, G. J., and Barton, J. C.: Ectopic Pelvic Kidney, J. A. M. A. **106**:197-199 (Jan. 18) 1936.

4. Woodruff, S. R., and Scherer, R. G.: Renal Ptosis, J. Urol. **35**:125-134 (Feb.) 1936.

also divided in the line of the incision. This in turn exposes the fascial triangle, with the kidney directly beneath it. The internal oblique and transversalis muscles with their fascia are cut anteriorly as much as is necessary for good exposure. Posteriorly, the quadratus lumborum muscle is kept intact. The fascia of Gerota and the perinephritic fat are incised and completely stripped from the kidney. The skin and subcutaneous portion of the curved incision are grasped with suitable tenacula and undermined with a scalpel, so that the last two ribs with their intercostal muscles are well defined. The kidney is then retracted anteriorly so as to expose its posterior surface, and the capsule is nicked with a sharp-pointed scalpel held with its blade flat. The point of entrance should be about 2 cm. below both the outer and the superior renal margin. A grooved director is passed under the capsule, lifting it from the renal cortex, and the capsule is incised on the director. The line of incision runs from the superior renal pole to the inferior renal pole at this distance of 2 cm. from the renal periphery. This loosened capsule is then stripped down toward the renal pedicle, exposing an area of renal tissue. When the kidney has been prepared, three mattress sutures of no. 2, forty day chromic catgut are then passed through the substance of the kidney along the periphery of the denuded area of the capsule, one in each end of the kidney and one halfway between them. Each suture thus forms a U, with the closed end on the anterior surface of the kidney and the upright ends penetrating the substance of the organ about 1 cm. apart. A straight blunt needle, 3 inches (7.6 cm.) long, is used when passing the suture through the kidney and muscles. In placing the sutures, the upper strand of the first mattress suture is carried well above the last rib under the direction of the operator's hand, in order to avoid puncturing the pleura or the liver. The second strand is then placed in the same manner somewhat medial and inferior to it. The second suture usually spans the twelfth rib, or in some cases it may also be placed above this rib. The third mattress suture will usually be placed below the twelfth rib and in the quadratus lumborum and the erector spinae muscles.

Woodruff and Scherer reported a series of 65 cases in which this operation was performed. Thirteen of the patients (20 per cent) were males, and 52 (80.1 per cent) were females. Twenty-one (32 per cent) had had previous major abdominal operations without any measure of relief from the symptoms of which they complained and for which the operation was performed. All 65 patients had medical treatment of some sort without experiencing relief, and 22 (33.9 per cent) had medical treatment of various types over long periods of time with the same result. On examination 20 (30 per cent) had palpable renal ptosis. Roentgenographic examination before operation of 26 patients (40 per

cent) revealed the presence of caliectasis, pelviectasis or ureterectasis alone or in combination. In 19 of these the dilatation was of grade 2; in 4, of grade 3, and in 3, of grade 4.

The results after operation by the method of Woodruff and Scherer were as follows: Six (9.2 per cent) of the patients could not be traced; 55 (93 per cent) patients were completely relieved; 3 (5.3 per cent) had been definitely helped, and 1 patient (1.7 per cent) was not relieved by operation. Of the 65 patients, 48 (74 per cent) had pyelograms or excretory urograms made at varying periods after operation. The kidneys of the 48 patients were maintained in excellent position, i. e., the position in which each was fixed at operation.

Birdsall [5] found that the operation described by Kelly and Brodel was the most satisfactory for anchoring the kidney in its correct anatomic position. Three sets of triple mattress sutures of no. 1 chromic catgut are introduced through the capsule on the posterior surface of the kidney, the upper set being inserted through the capsule of the upper pole of the kidney and the second and third sets through the capsule of the middle and lower poles, respectively. The kidney is then placed in its new bed, its proper position is determined and the fixation sutures are introduced so as to maintain this object. It is essential to place the kidney so that free drainage is accomplished, and this can be done by fixation of the upper pole of the kidney at a point closer to the spine than the lower pole. The upper sutures are, in most instances, brought through the intercostal muscle between the eleventh and the twelfth rib; the second and third sets of sutures are introduced immediately below the twelfth rib and through the erector spinae muscles. The introduction of the fixation sutures is best accomplished by the use of a long, curved Reverdin needle. By this technic, the kidney is fixed in as high and correct an anatomic position as it is possible to obtain; its posterior surface is in direct contact with the lumbar muscles, and there is no possibility of rotation, as is the case when its convexity is sutured to the edges of the incision.

By this method of suspension, nephropexy was performed by Birdsall in 57 cases of unilateral and in 9 cases of bilateral nephroptosis, making a total of 75 kidneys suspended. The end-results obtained were excellent in 73 kidneys. In 2 kidneys the operation failed; in 1 of these the technic in the introduction of the sutures was faulty, and in the other marked hydronephrosis was present. This kidney became infected, pyelonephritis developed and nephrectomy was necessary. Pyelograms, made with the patient in the erect position, after nephropexy, have been taken of 26 kidneys, and in each case the position of

5. Birdsall, J. C.: The Symptomatology, Renal Pathology, and Treatment of Nephroptosis, J. Urol. **35**:135-155 (Feb.) 1936.

the kidney was excellent, and there was no apparent advancement of renal destruction. After nephropexy it is essential that the patient be kept in bed in the recumbent position long enough for firm adhesions to form and hold the kidney securely in place in its new and permanent situation. The patient is kept in the dorsal position the first week, but may be turned on the side on which operation was performed the second week and allowed to sit up in bed at the end of the fourth week. Many patients complain of vague pains and regions of anesthesia for several months after the operation. An abdominal support is not necessary.

Tumors.—Pohle and Ritchie [6] reported 6 cases of malignant tumor of the kidney in children. The mixed tumor occurs chiefly in children usually less than 10 years of age, though it is sometimes found in adults. It not infrequently occurs bilaterally and may be found in any part of the kidney. The size varies with the age of the growth at the time of its discovery. The tissue of the tumor is usually sharply demarcated but may be infiltrative. The gross structure is extremely variable and may include hemorrhage, necrosis and cartilage or the formation of bone as special features.

Tumor of the kidney in children generally does not produce symptoms until the growth has reached considerable size. In contrast to hypernephroma, this highly malignant neoplasm seldom causes hematuria early in its course, and the absence of pain also tends to prevent its early discovery.

The diagnosis of a fully developed tumor of the kidney in a child is usually not difficult. In the differential diagnosis, pyelography and intravenous urography are important aids. If sufficient tissue of the kidney has been destroyed, the involved side is not visualized after the intravenous injection of the dye.

The prognosis of tumor of the kidney in children is unfavorable. Although occasionally a patient may survive, the available data indicate that the mortality is more than 90 per cent. In 17 of a total of 163 cases of neoplasm of the kidney the growth was classified as Wilms' tumor; only 1 of the 17 patients survived operation by a few years.

Before the advent of high voltage roentgen therapy, the treatment of tumor of the kidney in children was entirely surgical. Since such a tumor is composed largely of embryonic tissue, it may be assumed that it is radiosensitive. Marked reduction in size may be brought about by roentgen therapy. As soon as the tumor has been reduced to such an extent that it is barely palpable and provided the general condition of the patient is satisfactory, removal of what remains of the tumor may be attempted. The technic of treatment is simple. Usually

6. Pohle, E. A., and Ritchie, G.: Malignant Tumors of the Kidney in Children, with a Report of Six Cases, Radiology **24**:193-203 (Feb.) 1935.

exposure of one anterior and one posterior field suffices; if the tumor is large, a third lateral field can be exposed. The question of dosage is a matter of debate. Even with relatively small doses, violent systemic reactions, sufficiently severe to force interruption of the treatment, occurred. The poor general condition of the patient, when the blood count is low, also renders moderate or small doses advisable. If pain is severe, roentgen treatment may be palliative and is therefore indicated. Treatment of metastatic lesions in the lungs is not recommended, although, theoretically, they should respond because of the radiosensitivity of the primary tumor.

An analysis of these 6 cases of tumor of the kidney revealed a high degree of malignancy. Operation alone or combined with irradiation seemed ineffectual in eradicating the disease. A striking temporary improvement was followed soon by either a local recurrence or widespread metastasis, which led to death. The lungs seemed to be the most frequent site of secondary involvement.

It has been observed that a tumor may almost completely disappear after roentgen therapy, so that palpation will not definitely reveal any mass in the region of the kidney, but laparotomy often reveals the presence of a moderately large residual tumor. In the authors' experience, preoperative irradiation did not in any way complicate the surgical procedure. It was an unexplainable fact that the only surviving patient had received roentgen treatment solely; the tumor was not removed, nor was nephrectomy performed. In spite of this case, Pohle and Ritchie expressed the belief that preoperative irradiation and removal of the residual neoplasm, followed by postoperative irradiation, are the most satisfactory method of treatment.

According to Braasch and Griffin,[7] carcinoma of the renal cortex may be divided into two types which have distinct clinical characteristics, namely, adenocarcinoma (hypernephroma) and alveolar carcinoma. Metastasis occurs most frequently with renal tumors of the higher grades of malignancy and may be present without causing clinical evidence. Lymphatic extension occurs frequently. Metastasis is found most often in the lungs and rarely in the osseous system. Although the progress of the disease in the presence of pulmonary metastasis may be delayed by nephrectomy and irradiation of the lungs, postoperative results indicate that the chance for recovery is so slight that operation is not justified. Calcification of tissues in cases of renal adenocarcinoma is a frequent occurrence and indicates a favorable

7. Braasch, W. F., and Griffin, Miles: The Prognosis in Renal Carcinoma and the Clinical and Pathologic Data Affecting It, J. A. M. A. **106**:1343-1346 (April 18) 1936.

prognosis. Urographic evidence of widespread involvement of all calices and of the pelvis indicates a high grade of malignancy and a guarded prognosis.

Although clinical data suggest that adrenal elements may be included in some hypernephromas to account for the vascular manifestations, such as hypertension and telangiectasis, neither chemical analysis of the tumors nor postoperative clinical data corroborate such an assumption. Although the size of the tumor alone has no bearing on the late postoperative results, a large, fixed tumor, together with a history of short duration and evidence of marked toxemia, indicate that the prognosis is unfavorable and that the advisability of operation is questionable.

Bond [8] reported that in 176 cases of carcinoma of the genito-urinary tract in which treatment was given, complete follow-up data were available in 156 (90 per cent). Only cases in which the existence of carcinoma was definitely proved microscopically are included in the computation of results. Fifty-one cases in which the diagnosis clinically was carcinoma were rejected because microscopic material was not available. The number of proved cases considered in this report is 118. There were 14 cases of renal tumor. In 5 of these the growth was an adenocarcinoma with granular cells and in 5 a papillary carcinoma with clear cells. In 12 of the 14 cases hematuria was the main symptom. The duration of the hematuria varied from four days to eight years before the patient was examined. The epidermoid carcinoma was associated with renal calculi; the duration of life after nephrectomy was eighteen months. Death was due to extensive local recurrence. The treatment in all cases was nephrectomy. Roentgen rays and radium were used in only 1 case. Six patients (43 per cent) lived five or more years after treatment. One patient was alive and well twelve years after treatment; 1, ten years; 1, nine years, and 1, five years. One lived nine years and died from pneumonia; another lived six years and died from the same cause.

There were 63 proved cases of carcinoma of the bladder. This was after exclusion of 28 cases which were rejected because of insufficient microscopic data. In 45 per cent of the cases of carcinoma of the bladder the growth was of the epidermoid type; in 29 per cent, it was a papillary carcinoma and in 16 per cent, an adenocarcinoma; in the remaining 10 per cent, the growth was a scirrhous, medullary or cellular carcinoma of undetermined histologic type. In 47 cases (76 per cent) the chief symptom was hematuria. According to the patients' statements, this had been present for from eight days to twenty-five years.

---

8. Bond, F. T.: Experiences with Renal and Vesical Carcinoma, J. Urol. **35**:309-315 (March) 1936.

In 7 cases the bleeding had existed for more than six years. The treatment in these cases was undertaken with the intention of resection or excision if such a procedure was physically possible. In practice, the tumor usually was so extensive, involving the ureter and trigon, that resection was possible only in 6 cases and excision in 6 others. In 24 cases the treatment consisted of cystotomy, fulguration of the tumor and implantation of radon seeds. The results of treatment follow: Seven patients (11 per cent) lived five years or longer; 2 patients were alive and well after eleven years, 1 patient after eight, 1 after seven and 1 after five; 1 patient lived ten years and another seven years, and neither died from carcinoma.

Counseller and Menville [9] stated that benign tumor of the kidney is extremely rare, and even when present, it seldom gives rise to symptoms which necessitate surgical intervention. Among the benign growths which have been encountered in the kidney are adenoma, lipoma, fibroma, myxoma, myoma, hemangioma, lymphangioma and chondroma. The authors present a case in which nephrectomy was required because of two benign lesions in the lower pole of a kidney that also had duplicate pelves. A woman aged 29 noticed a painful tumor in her left flank six months prior to examination. Mild frequency, dysuria and hematuria had occurred. Roentgenographic studies of the left kidney showed marked deformity characterized by upward and medial displacement of the pelvis, flattening and obliteration of the lower calices and flattening of the lower border of the pelvis. The lesion was thought to be a cyst or a tumor. The right kidney was normal. At the time of operation a large cystic mass was found in the lower pole of the kidney. The cyst was opened and evacuated, and an irregular mass suggestive of a malignant growth was found at its base. Nephrectomy was performed. Pathologic study of the kidney revealed a large cyst of the lower pole containing a mass of spongy tissue with the histologic characteristics of leiomyoma. Because of the proximity of the tumor to the pelvis and calices, it was thought that it might have originated in the smooth muscle of a calix or of the pelvis. No evidence of malignancy was noted.

Stone.—Cifuentes [10] stated that bilateral reno-ureteral lithiasis occurs more frequently than is generally believed; it affects about 20 per cent of the patients with renal lithiasis. This is because the intrinsic disease (diathesis, metabolic disturbances, etc.) does not act at random

9. Counseller, V. S., and Menville, J. G.: Leiomyoma Associated with Benign Cysts in a Kidney with Duplicate Pelves, J. Urol. **35**:253-258 (March) 1936.

10. Cifuentes, Pedro: La litiasis reno-ureteral bilateral (Estudio clínico e indicaciones en su tratamiento), Madrid, Grafica Universal, 1935.

on one kidney alone but affects the two kidneys, both of which are subjected to the same disturbances and in an identical way.

In most cases the evolution of the disease runs a latent course in one or in both kidneys, and the calculi reach a considerable size before symptoms appear; pyuria is often the only clinical manifestation until roentgenographic examination reveals that the condition is bilateral.

When operation is performed it should be done in two sittings, one or two months apart. Generally speaking, the kidney that is least affected should be the first operated on, the stone being removed by simple pyelotomy. This insures improved function of one kidney and permits greater freedom in surgical intervention on the other kidney at a later time. If, however, the condition of the more seriously impaired kidney constitutes a danger to life, this kidney should be the first one operated on, treatment of the sounder kidney being left until later. If there is a ureteral stone on one side, this side should be operated on at the outset, to overcome the danger of a sudden blockade of the ureter. If calculi are present in both ureters, an attempt should be made to remove them by ureteral catheterization when their size permits. If this is impossible, ureterotomy should be done first on the side that has more recently been obstructed, provided the stone on the other side is well tolerated.

The presence of renal insufficiency revealed by functional tests is not an absolute contraindication to operation; it may be possible by suitable urologic treatment to improve the function and to save at least one kidney.

In treating bilateral lithiasis, three fundamental principles should be observed: 1. Abstention from operation, in the presence of evident contraindication, in many cases in which tolerance has been established will enable a patient to survive for a long time. Under such conditions, only the occurrence of a grave, acute accident should lead the surgeon to perform an emergency operation. 2. In a substantial number of cases operation should be done on one side only, to conserve a kidney that guarantees good function, with abstention from operation on the other kidney in cases in which this has attained a certain degree of tolerance and in which intervention might mean a risk for the patient. 3. Nephrectomy should be resorted to in cases of bilateral lithiasis only in exceptional instances.

Not infrequently lithiasis appears in the second kidney after the condition has been observed or after operation has been performed on the assumption that the disease was unilateral. This occurred in 13 per cent of the author's cases. This is one of the most tragic situations that may occur in pathologic changes in the urinary tract because of the anuria that appears on the occasion of the slightest nephritic colic

and for which ureteral catheterization, ureterotomy or nephrotomy must be promptly performed. For this reason one may well hesitate to perform nephrectomy if a stone is present in one kidney.

As recurrence frequently occurs after conservative procedures, the opposite kidney should not be removed even for severe infection or extensive calculosis unless it is certain that the other kidney has been completely cured and that further stones are unlikely to develop.

Anuria in a patient with lithiasis, even when he presents a syndrome affecting only one side, should make the urologist regard the lithiasis as really bilateral. This is why it is always an extremely grave symptom, for which ureteral catheterization should be done without delay and nephrostomy carried out while there is still hope for its success.

Counseller and Hoerner [11] stated that nephrostomy is a surgical procedure that has been in use for many years, but only comparatively recently have advances been made which have widened its field of applicability. A review of 209 cases of large or multiple renal stones in which operation was performed from 1929 to 1933, inclusive, is presented. This period was selected because it coincided with the time that nephrostomy began to be more frequently employed at the Mayo Clinic in the treatment of these conditions. A diagnosis of unilateral stone was made in 164 cases and of bilateral stones in 45. Of the 45 patients with stone in both kidneys, 21 underwent bilateral and 24 unilateral operation. In some of the cases in which the condition was bilateral, operation was performed on one side only because the stones in the other kidney were less than 5 mm. in diameter and complications were not present.

Simple pelviolithotomy often gives satisfactory results in the presence of large renal calculi. In such cases renal function returns rapidly subsequent to the release of the obstruction. In some cases it is frequently difficult to determine whether adequate drainage will be obtained without nephrostomy. One of the chief indications for nephrostomy is in calculous anuria, in which case it is necessary to establish temporary diversion of the urine. The obstruction may be relieved at the same time, provided the condition of the patient warrants it. Nephrostomy may also be advisable in the presence of chronic, partial obstruction that has produced a variable amount of injury to renal tissue. Although infection cannot be demonstrated in some of these cases before operation, not infrequently it becomes a serious complication after operation. It is possible in such cases that operation may have stirred up a latent process or that contamination occurred at the time

11. Counseller, V. S., and Hoerner, M. T.: An Analysis of the Effectiveness of Nephrostomy in the Treatment of Large Renal Calculi, J. Urol. **35**:21-31 (Jan.) 1936.

of the surgical procedure. Under the circumstances, nephrostomy promotes a smoother convalescence by providing better drainage. When infection is known to exist in conjunction with chronic obstruction, the function of such kidneys is always uncertain, as present diagnostic aids under these conditions are not reliable. Not infrequently an apparently functionless kidney will be found at operation to contain a considerable amount of valuable renal tissue. Proper drainage by nephrostomy facilitates the eradication of the infection and the return of function of the remaining renal tissue to its full capacity. There is another type of renal lithiasis in which large stones fill both pelves and are not removable by present surgical methods. Although these calculi may produce no symptoms, they gradually destroy renal tissue and eventually lead to a fatal outcome. Nephrostomy will maintain satisfactory renal function for years in such cases.

Permanent nephrostomy is reserved for cases in which the underlying pathologic condition cannot be remedied satisfactorily. Drainage by temporary nephrostomy is maintained for a variable period, depending on the condition of the kidney at operation and subsequent evidence of improved function and diminished infection.

Nephrostomy has several significant advantages over pyelostomy. Retention of a catheter in the pelvis of the kidney for more than one or two weeks after pyelostomy is difficult, and when it is necessary to change the tube because it has become obstructed by débris, replacement of the catheter is often troublesome and sometimes impossible. Drainage through the cortex is more effective than through the pelvis, for a catheter in the pelvis may prolong the irritation of the mucous membrane. There is probably less tendency to this with nephrostomy. Pyelostomy is favored by some surgeons because it does not destroy renal tissue. Nephrostomy can be done with little injury to renal tissue, and the catheter can often be placed in the wound through which the stone was removed. One of the important advantages of nephrostomy is the fact that there is much less danger of renal fistula.

Fifty-nine cases in which nephrostomy had been performed and 86 cases in which it had not were compared as to results. Improvement of the original pathologic condition was noted in 48 per cent of the cases in which nephrostomy was performed but in only 25 per cent of the cases in the other group. There was a negligible and insignificant difference in favor of the group in which nephrostomy was not performed in regard to recurrent stones and improvement of hydronephrosis and in the pathologic condition of the kidney. Subsequently, nephrectomy was required in 6.8 per cent of the cases in the group in which nephrostomy was performed and in 1.2 per cent of the other group. It was noted that the original pathologic condition was definitely more serious in the group in which nephrostomy had been performed.

TUBERCULOSIS

Papin, Goidin and Busser [12] pointed out that the pathogenesis of the caseous form of renal tuberculosis is always obscure and that it has never been possible to reproduce it experimentally. Attempts to do so have always resulted in the granular form. While it appears indisputable that the invasion of the kidney has taken place by way of the blood stream, it is impossible to explain why the lesions assume a special character in the forms which have with more or less reason been called "surgical tuberculosis of the kidney." A lymphatic theory of their origin does not account any better for the fact that renal tuberculosis begins in the medullary portion of the kidney.

As an aid in clarifying the pathogenesis of caseous tuberculosis of the kidney, the authors presented a case in which the lymphatic origin of the lesions seems beyond dispute. When the left kidney, which had been removed, was examined, three small well defined nodules, each about 1.5 cm. in diameter, were observed at the ischemic upper pole, literally within the lips of the hilus and at its base, flush with the intrahilar fat and slightly encroaching on the adjacent renal parenchyma. Histologic examination revealed that all three were typical tuberculous nodules, caseated at the center and bordered by a layer of epithelioid and lymphoid cells. Although the nodules were adherent over a small amount of surface to the renal parenchyma, which was more or less infiltrated by granulation tissue, the greater part of each one was surrounded by the hilar fat, which was likewise infiltrated with inflammatory elements. On one of them, near the axis of a blood vessel, was a small aberrant group of tuberculous follicles and also a center of caseation which had reached and surrounded the wall of a fair-sized artery, causing the musculo-elastic layer to undergo caseation with more or less tendency of the lumen to become obliterated. Adjacent to another of the nodules there was a small lymph node crowded with tuberculous follicles. Small amounts of inflammatory infiltrates were found moderately disseminated through the renal parenchyma, generally near the vessels, and there was ischemic necrosis of almost all the cortical zone contiguous to the tuberculous nodules. No tuberculous follicles were found at any distance from these nodules beyond the small mass.

The ensemble of lesions is suggestive, not so much of common renal tuberculosis as of tuberculous adenopathy of the hilus, with invasion of the renal tissue from the lips of the hilus, associated with secondary vascular lesions which had led to ischemia of the cortex through obliteration of the lumen of the artery. It was this rather unusual mechanism of production that led the authors to report the case.

12. Papin, E.; Goidin and Busser: Tuberculose rénale secondaire à une adénopathie tuberculeuse hilaire, Arch. d. mal. d. reins **9**:197-203 (March) 1935.

Pugh,[13] in a review of cases of tuberculosis of the kidney in pregnant women, noted that abortion or nephrectomy was practiced in about 70 per cent of cases in which exacerbation of unilateral tuberculosis occurred during gestation. These facts suggest that conservative measures are definitely contraindicated. As the renal process is acutely exacerbated in practically all cases of obstruction, immediate intervention is urged. Interruption of the pregnancy fails to check the process of the disease and is dangerous, particularly in the later months. This procedure should be resorted to only when the patient refuses nephrectomy or when infection of both kidneys is present.

From the evidence reviewed the conclusion may be drawn that pregnant women stand the operation of nephrectomy particularly well; in fact, it seems no more serious than when attempted on women who are not pregnant. All of 18 patients on whom nephrectomy was performed recovered. In 5 cases in which operation was not performed the condition was serious; in 2, death occurred late in pregnancy. It is a well recognized fact that children of tuberculous parents are particularly susceptible to infection by the bacillus of tuberculosis, not by placental transmission but because they are good culture mediums. Stevens,[14] quoting Morris, stated that the average mortality is approximately 60 per cent among children born of tuberculous mothers. It is therefore to the advantage of both mother and child to proceed with early removal of the tuberculous focus of infection. Matthews, in 1921, in a study from the literature of 265 pregnant women on whom nephrectomy was performed, found that labor of 200 was normal and of 15 complicated, with 2 deaths.

Schistosomiasis.—Stevens [14] reported a case of infection of the upper part of the urinary tract with Schistosomum. This was a rare case of renal involvement and was unusual because the lesion was a papillary growth of the pelvis and calices, which in this case seemed to have been the primary involvement of the urinary tract. The left kidney, which was eroded, together with about 7 cm. of ureter, was removed intact extraperitoneally. The ureter was split open, and a pedunculated papilloma more than 1 cm. in diameter was found about 4 cm. from the pelvis. The latter was largely filled with a papillomatous growth. Later the kidney was sectioned, and similar growths were found widely scattered over the walls of the hydronephrotic sac. The pathologic diagnosis was papillary epithelioma of the pelvis of the kidney, but

13. Pugh, W. S.: Tuberculosis of the Kidney in Pregnancy, J. Urol. **35**:160-171 (Feb.) 1936.

14. Stevens, A. R.: Schistosomiasis Involvement of the Upper Urinary Tract: Report of Patient with Papillomata of Renal Pelvis, Ureter, and Later of Bladder, Tr. Am. A. Genito-Urin. Surgeons **28**:275-283, 1935.

the gland gave evidence only of lymphoid hyperplasia, with no evidence of metastasis. Convalescence of the patient was uneventful. Later the remaining part of the left ureter was removed with the adjacent wall of the bladder, and a portion of the bladder containing the group of small papillomas was resected. Histologic examination of the tumors of the ureter and bladder revealed a papillary growth in association with which were numerous ova, some of which presented a terminal spine. A restudy of the tumors of the kidney was then made, and in one section a definite ovum was found. The patient made an uneventful recovery.

Hager [15] stated that schistosomiasis is a general term which implies an infection with any of the blood flukes or trematodes, of which there are three species that are pathogenic for man, namely, Schistosomum japonicum, Schistosomum Mansoni and Schistosomum haematobium. They differ primarily in their geographic distribution, in their selective localization within the human host, in their requirement of a specific mollusk for their intermediary metamorphosis and in their respective ova. S. japonicum is the oriental genus, confined mainly to Japan and China. It causes symptoms in the lungs and liver. The bladder never becomes involved; so it is of no particular concern to the urologist.

S. Mansoni and S. haematobium are both common to Africa, where schistosomiasis is widespread in many sections. S. Mansoni exists in the western hemisphere. It may be regarded as a heritage from the slaves and it has remained limited to the West Indies and certain localities in South America where conditions favorable for the completion of its life cycle obtain. The presence of the necessary intermediary host, therefore, limits the geographic distribution of the disease. Man is the only definitive host in which maturation of the worm takes place. Although certain laboratory animals have been infected experimentally, there is no evidence to show that they become infected in their natural state. S. Mansoni has a predilection for the rectum and is characterized by rectal lesions. In Africa, where both forms of Schistosomum are prevalent, a double infection may occur in which infection with S. Mansoni occurs in the bladder as well as in the rectum. In the West Indies, where infection with S. Mansoni alone occurs, the bladder does not become involved.

Vesical schistosomiasis or bilharziasis is characterized by lesions of the urogenital tract, usually of the bladder. Two features in the diagnosis are particularly emphasized by Hager. The first is the use of an extract of cercariae for a cutaneous test. The second is the value of a roentgenogram in the recognition of vesical schistosomiasis. Myriads

15. Hager, B. H., in discussion on Stevens.[14]

of ova are expelled into the lumen of the bladder and are passed with the urine. However, not all of them are extruded into the bladder, as many of them become arrested in the submucosa, where they undergo calcification. The calcified ova in the tissue cast a characteristic shadow on the roentgenogram which is pathognomonic of bilharziasis. In bladders in which the process has been extensive, there is a vague opacity that more or less outlines the periphery of the bladder which might be compared to the shadow cast by a fetal head. When calcification in the lower part of the ureter is marked, a mottled shadow of the dilated ureter can be demonstrated. Intravenous urography is particularly useful in the demonstration of obstructive uropathy, because of the difficulty of instrumentation incident to the distortion and formation of fistula in the urethra. Antimony and potassium tartrate is a specific for the disease. It kills the parasite, and it also destroys the eggs which have been deposited in the tissue. Christopherson, who introduced this drug, suggested a course of 30 grains (2 Gm.) given in solution intravenously over a period of from twenty-eight to thirty days.

Cysts.—Lindenfeld,[16] in a study of solitary cyst of the kidney, found reports of only 257 cases recorded in the literature, from which it must be concluded that the condition is rare. Since 1931, 5 cases have been recorded in his clinic in Krakow, on which he has based his article. Every cystic formation in more or less intimate contact with the kidney or its integuments is a cyst of the kidney, regardless of its histologic picture, the establishment of its renal structure or the presence of an epithelial lining. The sole criterion which shows that it belongs to the kidney is its localization, according to Lindenfeld.

Classifications of solitary cysts of the kidney have had little uniformity and many contradictions. Lindenfeld adopts the classification of Israel, with slight modifications, as follows: (1) intraparenchymatous cyst, (2) subcapsular cyst, (3) pararenal cyst and (4) parapelvic cyst (situated in the hilus). The majority of cysts treated surgically have belonged in group 2; that is, they have reached the external surface of the kidney at a certain time in their development, after starting within the renal parenchyma.

The etiology and pathogenesis are not yet known, but such a cyst is probably of embryologic origin. It is surprising to note that all authors apparently agree in identifying the pathologic anatomy of the solitary cyst with that of cystic kidney, holding that the same factor produces now a large cyst and now a cystic kidney and that there is only a quantitative difference. Lindenfeld does not agree with this idea. Solitary cyst is only a benign condition in an excellent degree, its very

16. Lindenfeld, L.: Kystes solitaires du rein. Étude clinique et expérimentale, J. d'urol. **38**:506-517 (Dec.) 1934; **39**:18-35 (Jan.); 119-130 (Feb.) 1935.

existence often being discovered only by accident. It endangers neither life nor the kidney, which for the most part remains functionally unimpaired. Cystic degeneration of the kidney as a rule (in 80 per cent of cases) is a bilateral condition and often is hereditary. In the adult it appears in a form comparable to nephrosclerosis and may even cause death by uremia. The two conditions, cysts and cystic degeneration, are entirely unrelated. The solitary cyst of the kidney consists of a kidney with a cyst; the cystic kidney is a large kidney honeycombed with small cavities, like a sponge. In the former, the parenchyma is sound; in the latter, destruction has begun and terminates fatally. In the solitary cyst, the epithelial lining is often wanting; in the cystic kidney it is present and in a state typical of degeneration.

Lindenfeld's explanation of the embryologic origin of the solitary cyst of the kidney is, briefly, that the kidney develops from two buds, both from the mesoderm: the secretory portion from the blastema of the kidney and the excretory portion from that of the ureter, which latter is also the germ of the primitive renal pelvis. The excretory ducts undergo a frequent division and push, as they grow, into the tissue of the blastema of the kidney, which they surround. This tissue is, so to speak, torn by the process and becomes subject to detachment and displacement, thus giving origin in rare cases to what will become a cyst in its later development. The cyst thus formed grows toward the surface of the kidney, and then, becoming free from the pressure of the surrounding parenchyma, finds conditions more favorable for its continuous development.

On the basis of this view, Lindenfeld performed experiments on animals to produce artificially the analog of a congenital cyst. After removing one kidney, he took pieces of its mucosa and transplanted them to the remaining kidney, at the same time, for purposes of comparison, grafting into the kidney pieces of another mucosa, that of the gallbladder, for which reason he also performed cholecystectomy on the animals; in some of them he also applied pieces of striped muscle as a control. The animals were kept under observation for from five to one hundred and eighty days. The results revealed that cysts developed in 70 per cent of the animals which had received subcapsular transplants of mucosa from the urinary tract; mucosa from the gallbladder also produced cysts, but of a different character. It appears, therefore, that the view that a solitary cyst of the kidney may arise from the detachment or the unlacing of a part of the germs of the excretory system of the urinary tract is well founded.

The only proper treatment of these cysts is surgical. Puncture is not satisfactory, since in 50 per cent of such cases the termination is fatal. The old method of incision left fistulas and is justifiable only

if there is suppuration of the content of the cyst. The ideal treatment is enucleation of the cyst. This was easily accomplished in 3 of Lindenfeld's 5 cases. But sometimes there are such dense adhesions to the renal parenchyma that the latter is injured in the process; in such a case it is necessary only to suture the small wound thus made to obtain perfect hemostasis. If the cyst extends to the bottom of the parenchyma, partial nephrectomy may also be unavoidable, but the results have not been satisfactory, as fistulas remain. In view, also, of the dangers of hemorrhage from such resection, it may be necessary to remove the entire kidney under such conditions to stop the bleeding. But this should be done only in the rarest cases. If the kidney must in some cases be partly removed, resection *en collerette,* as performed by Albarran, Marion and others, would seem the best method. The best approach is by a lumbar incision. At the end of the procedure, nephropexy should be effected to prevent ptosis of the kidney into the cavity previously formed by the cyst. In conclusion, the most important point is stressed: that the kidney should be conserved whenever possible, when the cyst is removed, since the organ is, as a rule, healthy in these cases.

Hydronephrosis.—Blanc and Guérin [17] described an unusual case of bilateral hydronephrosis in which a pregnant woman was suffering from two different types of this condition, the one congenital and the other acquired as the result of a congenital predisposition through abnormal vascularization of the kidney. On the left side the hydronephrosis, unaccompanied by ptosis, involved only the pelvis and calices, which it had completely destroyed; it began at the level of the vascular band, without involving the ureter, thus showing that it was not of the primary congenital type; there was no doubt of the rôle played here by the anomalous vessel in its formation. According to the authors, there can be no congenital hydronephrosis that is not also a hydroureteronephrosis, that is, a dilatation of the entire excretory tree, a condition that was, on the other hand, present on the opposite (right) side in the case under consideration. The left kidney was removed when the patient was two months pregnant; six weeks later the right kidney, which was eliminating only 31 per cent of phenolsulfonphthalein both before and after nephrectomy on the left side, and which was therefore not compensating, was found on intravenous pyelography to be both ptosed and hydronephrotic with a ureter that was dilated and sharply kinked a little below the ureteropelvic junction. With a conviction that the prognosis was too grave if this solitary kidney with inadequate

17. Blanc, Henry, and Guérin, Pierre: Considérations sur un cas d'hydronéphrose bi-latérale chez une femme enceinte opérée de néphrectomie gauche et de néphropexie droite, J. d'urol. **39**:208-218 (March) 1935.

function were left in its abnormal position to be subjected to the inevitable compression that would result in the later months of pregnancy, besides the danger of infection from urinary stagnation, nephropexy was carried out on the right side when the patient was four months pregnant. It was the authors' view that this operation should be followed immediately by a therapeutic abortion, but from religious considerations this was not permitted by certain colleagues, and the pregnancy, not without serious misgiving, was allowed to go on to what proved after all to be a successful termination, although it was followed by a renovesical colon bacillus infection.

It is altogether probable in this case that if a diagnosis of congenital hydronephrosis of the right kidney had not been made at the time of nephrectomy on the left side and if there had been occasion to take a pyelogram in the sixth or seventh month of pregnancy, the case would have been regarded as a perfect example of ureterohydronephrosis of pregnancy. The authors expressed the belief that a considerable number of cases in which the condition has been termed hydronephrosis of pregnancy were in fact instances of congenital hydronephrosis, merely revealed at the time of pregnancy.

The remarkably good results in this case, in which the hydronephrosis receded to a certain extent during the year after accouchement and in which the functional capacity of the remaining kidney greatly improved must certainly be attributed to the nephropexy. The case clearly proves that pregnancy does not constitute a contraindication to operation. On the contrary, by freeing and straightening the ureter, thereby improving the conditions for evacuation of the urine, it was possible to prevent probable grave infection, since lavage of the renal pelvis could be carried out throughout the remainder of the pregnancy.

Notwithstanding these excellent results, the authors stated that if a similar condition should arise in their practice they would prefer not to take the risk that was here involved, but would unhesitatingly advise the interruption of the pregnancy at an early period.

Renal Glycosuria.—Wade [18] emphasized the difference between renal glycosuria and glycosuria that is the result of diabetes mellitus. He stated that renal glycosuria is a not uncommon cause of the presence of sugar in the urine. The criteria essential to the diagnosis of this condition are: (1) the presence of dextrose in the urine without other sugars or reducing substances, (2) the raising of the curve for blood sugar after the oral administration of dextrose from a normal fasting level of from 80 to 120 mg. per hundred cubic centimeters to 180 mg. or more half an hour later. This value for blood sugar then drops to

18. Wade, J. L.: A Consideration of Renal Glycosuria, Proc. Staff Meet., Mayo Clin. **11**:346-349 (May 27) 1936.

a lower level at the end of the second hour, and at the end of the third hour it is down to, or below, the normal fasting level. Sugar must appear in the urine in at least one specimen taken during the test. Glycosuria must accompany a normal level of blood sugar. Renal glycosuria may be continuous, or it may be intermittent or cyclic.

The diagnosis of renal glycosuria has been made in 146 cases. Males predominated in the series in the ratio of 3:1. Many of the patients had thought, or had been told, that they had diabetes mellitus and had taken insulin for some years prior to the time the correct diagnosis was made. In many instances the presence of renal glycosuria is undoubtedly never discovered as the condition is frequently symptomless. Questionnaires were sent to the patients in an effort to determine their state of health. Eighty-eight replies were received. In not 1 of the 88 cases did diabetes mellitus develop. This observation is in accord with other articles on this subject.

Lymphatics.—Jasienski [19] undertook to study more precisely than has hitherto been done the anatomic details of the lymphatics of the renal parenchyma, using young dogs for his experiments, since the lymphatics reveal the closest resemblance to those of man. Unlike other experimenters in this field, he injected the color dye in situ into the kidneys of living dogs, without even displacing the organs, so that the circulation continued to be normal; not until the entire amount of the dye had been introduced slowly and without the least pressure did he proceed to remove the kidney. In this way he succeeded in filling the lymphatics with coloring substance under conditions that were approximately physiologic.

The arrangement of the lymphatics in the parenchyma is so characteristic that it is impossible to confuse it with that of the blood capillaries, when a proper technic is used, but this presupposes not only the cutting of very thin sections but their immersion in water during examination, without which the finest of the lymphatics do not become visible. It was necessary to examine over 20,000 sections before clear results could be obtained, for until one is well experienced with the technic one may frequently inject the color dye into venules as well as lymphatics, a circumstance which has led to much confusion among the various authors.

In order to know the lymphatic system in its ensemble, it is necessary to note separately the character of the lymphatics of the capsule and those of each one of the elements composing the parenchyma. The capillary network of the capsule is composed of relatively large nodes, but the size is subject to considerable variation in the different sectors.

19. Jasienski, George: Les lymphatiques du rein sain, J. d'urol. **40**:97-123 (Aug.) 1935.

Examined under oil immersion, the numerous sinuous enlargements of the canals present the appearance of cylindric spaces which alternately enlarge and contract, and from which start short ramifications with clearly defined contours and irregular form. The abundant intracapsular network, the plexuses of which extend almost parallel to the surface of the kidney, communicates directly with the network of the parenchyma, its numerous canals anastomosing as they pass toward the latter. The size of the meshes is subject to wide variations. Within the cortical substance every tubule, every glomerulus and every part of the blood vessels is surrounded with a rich lymphatic reticulum; the lymphatics even penetrate within the glomerulus as it accompanies the afferent vessel.

Outside of the hilus the collecting lymphatics of large caliber unite to form the trunks of the pedicle of the kidney, which are provided with valves; in addition, the network of the medullary substance communicates with that of the calices, pelvis and ureter.

Even under oil immersion the smallest lymphatic capillaries of the renal parenchyma are so extremely fine that their walls cannot be distinguished, but the uniformity of their contours and their characteristic undulatory appearance justified the conclusion that they are provided with these. A study of the large ones reveals a wide variety of form and shape, some being separated by large triangular spaces and others by rounded, oval or stellate spaces or spaces forming less geometric patterns. All these spaces intercommunicate by ramifications which create the multiform meshes of the network. They give off undulating branches, which are much finer than the blood capillaries and which cross the intertubular spaces and the tubules in all directions, without following them as do the arterial and venous capillaries. These characteristics, accordingly, distinguished the two vascular systems from each other. The blood vessels, too, the walls of which can be clearly distinguished here and there, are surrounded by a close-meshed lymphatic reticulum in a design that repeats itself regularly, and of which the most characteristic feature is the great number of enlarged spaces, which are provided with prolongations that sometimes make them resemble nerve cells. The character of the network depends on the caliber of the blood vessel it surrounds.

Injection into the lymphatic reticulum of the medullary substance of the kidney is attended by such great technical difficulties that it is successful only in exceptional cases. Jasienski succeeded a few times, by accident, in making intraparenchymatous injections in the superficial layers of the cortex which by chance carried the substance injected into small portions of the parenchyma. He was able, therefore, to see that

the surface of some of the straight tubules is covered with a rich network of lymphatics recalling those of the cortical substance, but it is much less fine and the anastomoses are less frequent than in the cortex, so that the meshes appear larger and seem to be prolonged in a vertical direction. Contrary to what is observed in other tissues and organs, the lymphatics of the renal parenchyma preserve neither their individuality nor their caliber for any great distance but are distinguished by a much richer arborization than that of the blood vessels. Everywhere there is a mixed network, with no large collecting trunk continuing over a single course, until the hilus is reached, when such trunks appear on the renal pedicle. All the pericapillary lymphatics pour their content into the perivascular networks. The respective networks of the capsule, cortex and medulla are not independent of one another: They constitute a single continuous system, composed of the ensemble of the small reticula which are in contact with all the histologic elements of the parenchyma.

Perirenal Lipomatosis.—Lieberthal,[20] in a routine examination of several thousand kidneys from surgical and postmortem material, found definite and significant changes in the perirenal and peripelvic fat in more than a hundred kidneys. From these he reconstructed chronologically the changes of perirenal and peripelvic fibrolipomatosis from the onset to the end-stage, the so-called replacement lipomatosis of the kidney. This is supposed to be a rare condition, but it is merely an advanced form of the peripelvic lipomatosis which accompanies every chronic suppurative process in the kidney. The changes in the peripelvic fat are secondary to the chronic inflammatory process present in the kidney, usually chronic or recurring pyelonephritis with atrophy and substitution of connective tissue.

Some authors assume that changes in the kidney are those of pressure from active proliferation and overgrowth of the peripelvic fat, but this is erroneous. Lieberthal gives illustrations of these changes, from early lipomatous hyperplasia (a hyperplasia ex vacuo) in the renal contracture of benign nephrosclerosis, chronic glomerulonephritis and chronic pyelonephritis to complete replacement lipomatosis, as seen in pyonephrosis caused by calculus.

The clinical significance of the changes lies in the altered renal topography, which makes operation on the kidney difficult at times. A detailed knowledge of these changes is essential to safe and expeditious operation.

---

20. Lieberthal, Frederick: Perirenal and Peripelvic Fibrolipomatosis: Their Relation to Replacement Lipomatosis of the Kidney, Surg., Gynec. & Obst. **61**: 794-801 (Dec.) 1935.

Nephro-Ureterectomy.—Papin and his associate,[21] after a glance at the history and a study of the anatomy of the region, reviewed the various technics for nephro-ureterectomy and described the routes of approach and the various incisions that have been used for accomplishing this combined procedure, together with the indications for each.

Among conditions that call for nephro-ureterectomy are the presence of calculi, when they have caused grave injury to both kidney and ureter, hydronephrosis and pyonephrosis, pyo-ureter, ureters with vesical reflux, cases of anomalies of the ureter and finally tumors involving the pelvis and ureter in which the entire reno-ureteral apparatus must be removed en bloc. With some reservation, renal tuberculosis may be regarded as suitable for this operation, but formal indications for this have been rare.

The long lumbo-iliac incision of Albarran and of Israel, used by most surgeons when a large kidney with large ureter has to be removed, runs from the twelfth rib (from the angle formed by it and the sacrolumbar mass) to the level of the anterosuperior iliac spine, at a point 2 fingerbreadths within it. Its disadvantages are the fact that the integrity of the abdominal and lumbar wall is injured, making suture of muscles in at least two planes necessary, and that many nerve filaments are cut, especially those from the tenth, eleventh and twelfth intercostal nerves; since these are motor filaments to the great oblique muscle, an incision too far forward may section filaments of the large and small abdominogenital nerves, it being impossible not to cut some of these branches. In addition, the two sides of the abdomen are left unequal, with the side operated on bulging. Although there may be no true eventration, there must always be weakness of the wall.

More satisfactory is the combined incision, that is, two incisions, one high and one low, leaving between them a strong segment of wall, as wide as possible. The upper incision is always a lumbar incision; it is sometimes the one first made, but often it follows the low incision. It should be made as short as possible, consistent with the size of the kidney. In order not to lose operating space at the upper end, the lumbocostal ligament must be cut close to the twelfth rib. When the lower incision, to free the ureter, has been closed, the patient is placed in the nephrectomy position. Then, after the lumbar incision has been made, it is possible to ligate and section the vascular pedicle at once and to extirpate the ureter from below upward; the ureter may first be extirpated and the renal pedicle tied afterward.

If the lumbar incision has been made first, without knowing in advance that a ureterectomy would be required, as, for example, when

21. Papin, E., and de Berne-Lagarde, Jean: Indications et technique de la néphro-urétérectomie totale et subtotale, Arch. d. mal. d. reins **10**:1-62 (Jan.) 1936.

a supposed tumor of the kidney turns out to be a tumor of the pelvis, one of the two following procedures may be carried out: 1. The kidney is removed, and the ureter is sectioned as low as possible between two ligatures; the lower stump is enveloped by a compress and solidly tied up with a silk or linen thread, and the wall is closed completely. 2. As soon as the necessity of removing the ureter is discovered, the lumbar wall may be closed only temporarily, with one or two skin sutures, a temporary dressing applied and the patient placed on his back while the pelvic incision is made for section of the ureter. The lower ureteral stump is prepared in just the same way, but through the pelvic incision, the ureter being separated as high up as possible; the pelvic incision is then closed, and the surgeon returns to the lumbar incision, to complete the operation by the usual technic. The latter procedure is long and tedious but has the advantage, in case of malignancy, of avoiding the section of a neoplastic organ.

Again, the lower part of the ureter may be reached by the hypogastric incision, which may take any of several forms, lateral, median, paramedian or mixed. The best known among these are the lateral incisions of Albarran, of Gibson and of Beer, the oblique incision of Gutierrez, the inguinal incision of Mazzoni and the various incisions devised by Herrick, Kidd, MacBurney, Pfannenstiel, Judd, Scholl and others. The incision most commonly used is that in the median vertical suprapubic line, from 12 to 15 cm. long, known in the United States as the incision of Judd. Whatever the technic for reaching the bladder by the median subperitoneal route, any of several procedures may be employed to expose the ureter, namely, (1) lateral décollement of the bladder, (2) total décollement of the bladder, (3) extraperitonealization of the bladder and (4) cystotomy, all of which are described.

For subtotal nephro-ureterectomy, the lumbar incision is always sufficient and can be prolonged downward according to need. The ureter is sectioned under full vision and as far down as possible between two ligatures or two clamps; Papin and his co-worker prefer the clamps. For a juxtavesical nephro-ureterectomy, the very long lumbar incision may be used, the only part of the technic that varies being at the lower segment of the ureter. 1. The entire ureter may be removed, and the vas deferens or the uterine pedicle sectioned, or if no adhesions are present, the ureter may be slipped upward from below, under these structures without cutting them. 2. The ureter may be removed in two segments, cutting it above the vas deferens or uterine pedicle and removing the lower segment separately, as may be necessary in case of calculus.

The authors concluded that the median route for exposure of the ureter has the most advantages, as follows: 1. In many cases the peritoneum need not be opened. 2. If necessary, the extraperitonealization

of the bladder gives an excellent exposure of the terminal part of the ureter. 3. If the bladder for any reason needs to be opened, there could be no more convenient route. 4. No other incision can compare with this one in its preservation of the solidity of the wall and the certainty of not injuring nerve filaments.

ADRENAL GLANDS

Adrenogenital Syndrome.—Broster [22] defined the adrenogenital syndrome as a condition in which secondary male sex characteristics appear in the female associated with retrogression of the primary and secondary female sex characteristics and their functions. The clinical picture is determined by the type of lesion and the age of the patient and is composed of the following abnormalities: the appearance of hair in females in masculine distribution; alterations in bodily contour resembling that of the male; immature development of the genitalia, both external and internal, and psychologic abnormalities.

The following classification of cases was made:

Group 1. Adrenal pseudohermaphroditism. This is the most complete form of the syndrome, in which changes occur before the bodily form and sex organs have become differentiated. There are marked virilism and hypertrichosis of the male type, primary amenorrhea, and normal feminine development has not taken place.

Group 2. Adrenal virilism. This later variety, in which the adrenal changes set in after puberty, is associated with alterations in bodily form, and in the external sex organs, hypertrichosis of the male type, and disturbance of sex functions. A relatively large number of patients belong in this group.

Group 3. The Achard-Thiers syndrome. The adrenal lesion appears to be one element in a multiglandular syndrome. These patients presented the symptom complex described by Achard and Thiers as "diabetes of bearded women." The chief symptoms are the male type of hypertrichosis of the face, obesity, glycosuria with decreased carbohydrate tolerance, hypertension, and usually amenorrhea, but without other signs of virilism.

From observations of 60 cases in which virilism in varying degrees was present, the author concluded that laboratory investigations usually give negative results and that the only method by which to detect adrenal hyperplasia is exploratory laparotomy. A subdiaphragmatic approach similar to that used for the kidney is employed. Patients subjected to unilateral adrenalectomy have evidenced no ill effects so far as their general physical condition is concerned, and there has been a definite tendency toward loss of hair and restoration of menstrual function. The largest adrenal gland removed measured 7.5 by 7.5 cm.; one of the smallest measured 4 by 2.1 by 1.5 cm. The author concluded

22. Broster, L. R.: Eight Years' Experience on the Adrenal Gland, Proc. Staff Meet., Mayo Clin. **11**:200-202 (March 25) 1936.

that virilism is not necessarily dependent on hypertrophy alone, as it may be associated with apparently normal adrenal glands.

Unilateral adrenalectomy was performed in 23 cases without a fatality. A specific differential staining quality in the cells of the adrenal cortex was found, which is evident in the reaction to the Ponceau-fuchsin stain. This quality is absent in controls but is present in the tumor cells in cases of virilism due to neoplasm. It was also present in the fetus of both sexes, and virilism can be explained by its abnormal persistence in the female. This abnormality, the author suggested, may account for the clinical syndrome evidenced by the patients in groups 1 and 2. He expressed the belief that in cases in group 3 the normal restrictive action of the pituitary body on the masculinating potentialities of the adrenal gland in the female may fail to be maintained. This type of case would then be associated with pituitary dysfunction, and the clinical picture would vary, depending on the predominance of one or the other factor.

Tumor.—Cahill, Loeb, Kurzrok, Stout and Smith [23] stated that tumors of the cortex of the adrenal gland may occur without virilism. The following endocrine changes may accompany their occurrence: pseudohermaphroditism (female); premature puberty in the male; growth maturity with masculinity in female children; hirsutism, amenorrhea and adiposity in adult females; an indistinct picture with adiposity after the menopause, and possible inversion changes in male adults.

Removal of a tumor of the adrenal gland by the transperitoneal route is the most satisfactory surgical procedure. In a certain percentage of cases collapse follows the removal of this gland. Removal of the tumor produces a symptomatic cure of the endocrine symptoms but has no effect on the anatomic changes in the pseudohermaphrodite. Metastasis of these tumors produces the same endocrine changes as the original growth. The tumor that produces the endocrine changes has cells which greatly resemble the reticulate layer of the adrenal gland and have an increase in fuchsinophilic granules over normal. The adrenal cortex hormone has not been demonstrated in these growths.

BLADDER

Tumor.—The Committee of Carcinoma Registry [24] reported 1,354 tumors in the registry in 1936; in 658 cases operation was performed

23. Cahill, G. F.; Loeb, R. F.; Kurzrok, R.; Stout, A. P., and Smith, F. M.: Adrenal Cortical Tumors, Surg., Gynec. & Obst. **62**:287-312 (Feb. 15) 1936.

24. Committee of Carcinoma Registry: Cancer of the Bladder; a Study of the Five-Year End Results in 658 Epithelial Tumors of the Bladder in the Carcinoma Registry of the American Urological Association, J. Urol. **35**:481-490 (April) 1936.

more than five years before. The record as to the final disposition of these 658 cases is complete, with the exception of 18 cases. Of the 658 patients operated on more than five years before, 151 were alive at the end of five years, a simple crude survival rate of 23 per cent. Of these 151 survivors, 104, or 15.9 per cent, were without evidence of disease by sign, symptom and cystoscopic examination. The remaining 47 survivors revealed some evidence of recurrence or metastasis.

There is nothing remarkable about the age or the sex incidence, but it has been found that among patients under the age of 50 years the tumor in both sexes was of high grade of malignancy in 50 per cent of the cases, whereas among the patients after the age of 50, carcinoma of low grade preponderated. There seems to be no relation between sex and grade.

Of the 151 patients who survived for five years, 37, or 24.5 per cent, had a tumor of grade 3 or 4, while 111, or 75.5 per cent, had a tumor of grade 1 or 2. The degree of malignancy of the tumor influences the end-result. Of 133 patients with a tumor of grade 1, 61, or 45.9 per cent, survived five years. Of 194 patients with a tumor of grade 2, 50, or 25.7 per cent, were alive at the end of five years. Of 244 with a tumor of grade 3, only 34, or 13.9 per cent, survived five years. Of 70 cases in which the tumor was of grade 4, in only 3, or 4.3 per cent, was the lesion under control at the end of the five year period. In the entire series of 658 cases, 312 tumors were known to be papillary, whereas 245 were classified as infiltrating. In the remaining 41 cases the lesion was not so classified. Of the 151 patients who survived for five years, 109 had a tumor classified as papillary and 34 as infiltrating, and the type of 8 of the tumors was unknown. Thus, of the 143 tumors that were classified, 34 infiltrating tumors, or 24.9 per cent, were controlled. The influence of neoplastic infiltration is further demonstrated by the result obtained in the papillary group and in the infiltrating group in the entire series. Of 312 patients with a papillary tumor on whom operation was performed more than five years ago, 109, or 34.9 per cent, survived five years, whereas of 245 with an infiltrating tumor 34, or 13.9 per cent, were cured. The size of the tumor when first seen is also related to the result at the end of five years. One hundred and twelve tumors were stated to be less than 2 cm. in diameter when first seen. Three hundred and nine varied from 2 to 5 cm. in diameter, while 222 were larger than 5 cm. in diameter. The size of 15 tumors was not stated. It is an interesting commentary on the usual delay in the diagnosis and treatment of tumor of the bladder that only 112 of the 658 patients, or 18.5 per cent, came under observation when the tumor was still less than 2 cm. in diameter. Yet it is in this very group that the largest percentage of five year cures was obtained, namely, 34 of

112 cases, or 30.3 per cent. When the tumor varied from 2 to 5 cm. in diameter, 82 of 309 patients, or 26.5 per cent, survived five years. However, when the tumor was larger than 5 cm., in only 35 of 222 cases, or 15.8 per cent, was the growth under control for five years.

The open surgical method, combined in the majority of cases with the use of physical agents, was the treatment of choice in 468 of the 658 patients. One hundred and forty-five patients were treated by closed methods without surgical intervention.

Of 468 patients operated on, 29 patients died after operation, an operative mortality for the series of only 6.2 per cent. Of 27 on whom partial resection of the bladder was performed, 7 died after operation, a mortality of 26 per cent. Cystotomy with excision of the tumor and without the use of physical agents was used on 105 patients, 5 of whom died after operation, a mortality of 4.9 per cent. Cystotomy with the implantation of gold radon seeds was used in 147 cases, after which 3 patients died, a mortality of only 2.05 per cent. Cystotomy with fulguration as the principal form of physical therapy was utilized in 121 cases, followed by 9 postoperative deaths, an operative mortality of 7.4 per cent. In 66 cases the bladder was opened, and the actual cautery was applied to the tumor, following which 4 patients died, a mortality of 6.1 per cent. The mortality in the closed methods of treatment was as follows: Of 54 patients treated by the cystoscopic implantation of gold seeds of radon, 2 patients died, or 3.9 per cent. After cystoscopic fulguration of 76 patients, 5 patients died, or 6.6 per cent.

In 27 cases in which partial resection of the bladder was done for tumor, 8 patients, or 29.6 per cent, survived five years. Of the 8 survivors, 3 were alive at the end of five years with recurrence or metastasis. Hence, only 5 patients, or 18.5 per cent, of the 27 so treated were entirely without evidence of disease by symptom and cystoscopic examination at the end of five years. One hundred and five patients were treated by cystotomy and simple excision of the tumor. Of these, 34, or 32.4 per cent, survived five years. Cystotomy with the implantation of gold seeds of radon was utilized in 147 cases, and 24 patients, or 16.3 per cent, were living at the end of five years. Only 13 patients so treated, however, were without evidence of disease at the end of five years (8.8 per cent). Cystotomy with fulguration was the method of choice in 121 cases. Of these, 30 patients, or 24.8 per cent, lived five years. Eighteen of the patients, or 14.8 per cent, were without cystoscopic evidence of disease at the end of that time. Of 66 patients treated by cystotomy and the application of actual cautery, 12, or 18.2 per cent, were alive at the end of five years, and 8, or 12.1 per cent, of these revealed no evidence of recurrence or metastasis.

Of 54 patients treated by the cystoscopic application of radium, 11, or 20.4 per cent, were alive at the end of five years. Of these 11, 8, or

14.9 per cent of all patients so treated, revealed no cystoscopic evidence of disease at the end of five years. Seventy-six patients were treated exclusively by cystoscopic fulguration. Of these, 29, or 38.2 per cent, survived five years. Twenty-five, or 32.9 per cent of the whole, were without cystoscopic evidence of disease at the end of five years. Fifteen patients in whom the condition was hopeless were treated by means of roentgen rays, and 2 survived five years, 1 without evidence of disease at the end of that time.

Quinby [25] stated that at the Peter Bent Brigham Hospital patients on whom total cystectomy has been performed have been chosen on the following criteria: The growth must be on the lower segment of the bladder so that its removal would involve the sphincter or orifice of the ureter or both; there must be no demonstrable metastasis to the regional lymph nodes or to those of the aortic area; on one side at least the excretion from the kidney, its pelvis and ureter must be normal, and, finally, microscopic examination must reveal evidences of actively growing carcinoma.

At the time of this report, 10 patients had been treated by total cystectomy and uretero-intestinal anastomosis. One patient, a woman, was alive more than three years after operation. There was no evidence of recurrence. Of the other 9 patients, 2 died as a direct result of operation which was imperfect in some way. The remaining 7 patients died of recurrent carcinoma at shorter or longer periods after operation. In none of these, however, was there any further acute difficulty in the urinary tract. The patient who survived the operation the longest lived for eight years after cystectomy. Until the last year of his life this patient had been well and active. Signs of recurrence of the malignant lesion then appeared in the region of the lower part of the rectum, and the man died about twelve months later.

From Quinby's experience with these patients, especially when comparing their postoperative careers with those of patients in whom carcinoma of the bladder has been treated by radium or various combinations of radium and partial excision, he concluded that total cystectomy should be employed more often than has been done in the past in the treatment of carcinoma of the bladder.

Keyes, Ferguson and Hocker [26] stated that a single tumor of the bladder which is of grade 1 or grade 2 malignancy may be satisfactorily treated by such methods as fulguration, implantation of radon seeds and resection. If the tumor recurs, it is classed as multiple. Multiple

25. Quinby, W. C.: Indications for and Results of Total Cystectomy for Cancer of the Bladder, New England J. Med. **212**:501-503 (March 21) 1935.

26. Keyes, E. L.; Ferguson, R. S., and Hocker, A. F.: Roentgenotherapy for Recurring Bladder Tumors of Low Malignancy: A Preliminary Report, Tr. Am. A. Genito-Urin. Surgeons **28**:265-269, 1935.

tumors recur after any treatment. It has been estimated that recurrence occurs in half the cases in which the tumors are multiple. Recently a form of roentgen therapy that does not cause roentgen sickness or grave irritation of the skin has been employed. Vesical rather than cutaneous sensitivity limits this treatment. Tumors of a low grade of malignancy and of slight cellular differentiation are especially vulnerable to this form of treatment.

Until recently, roentgen therapy has been applied to the full erythema dose. The usual dosage is as follows: 200 kilovolts, from 4 to 25 milliamperes, a filter of 0.5 mm. of copper and 1 mm. of aluminum and a skin-target distance of 50 cm. From two to four treatments are given at intervals of from four to seven days. Skin tolerance limits the treatment. Coutard has shown that excellent results may be expected if each dose of roentgen rays is reduced from 700 roentgens to 300 or 400 roentgens, exposure to the rays being repeated daily for eighteen or twenty days. By Coutard's therapy the effect on the surface is less, and the deep effect is greater. Thus roentgen ray sickness is less, but irritation of the bladder and of the bowel is considerable.

Ferguson determined on the following set-up: 200 kilovolts, 25 milliamperes, a filter of 1.7 mm. of copper and 1 mm. of aluminum and a skin-target distance of 100 cm. Four portals are employed, one over each rectus muscle and one over each buttock; these are to be irradiated in pairs each alternate day. The duration of irradiation is fifteen and a half minutes, whereby a dose of 100 roentgens is delivered to each portal. The total dose is 3,000 roentgens to each portal, more or less. By this method an increase of from 15 to 20 per cent in dose of effective radiation at a depth of 10 cm. is obtained. The treatment is continued for from forty-five to sixty days. The results with this method of treatment have been absence of roentgen ray sickness, relief of spasms of the bladder as far as they are due to tumor, checking of hematuria in the second or third week and minimization of cutaneous irritation. The irritation of the bladder is mild. If the patient is urinating about every hour, this irritation does not increase. This therapy has been applied to tumors in various parts of the body with comparable results. If cystoscopy is performed within a month after treatment, the mucosa will sometimes appear inflamed and sometimes normal. An effort has been made at intervals of two weeks during treatment to destroy the tumor. One day the tumor will be there, revealing some cellular disintegration, and the next day it will be gone.

Thirty tumors of the bladder were treated by irradiation in divided doses. Various modifications of Coutard's technic were employed until January 1935. Since then the author's own technic as described has been used in 12 cases. There was 1 relapse and no deaths; in 4 cases subsequent cystoscopy revealed no tumor, and 8 patients are doing well

but are still under treatment. Four of 30 patients had died, 1 was not relieved, 1 had a recurrence and 16 have been relieved from their symptoms and cystoscopy did not reveal a tumor.

Parmenter and Leutenegger [27] stated that hematuria, with or without vesical disturbance, is the cardinal symptom of tumor of the bladder. In their series it was present in more than 90 per cent of the cases. Fulguration seems to be curative in cases of benign papilloma. It is simple to apply and rapid in its effect and has slight morbidity and no mortality. Its use should be limited to benign papillomas, regardless of the fact that it is sometimes apparently curative in malignant conditions. In the cases in which the papilloma was malignant there were about the same number of five year cures when fulguration alone was used as in those in which fulguration and radium were used. The number of patients in the fulguration-radium division was numerically less by about 33 per cent. It was also noted that the length of life was longer in a greater number of these, that the effect on the tumor was more pronounced, that the recurrences were fewer and that the time interval between was greater. Fulguration alone, with its necessity for constant repetition, is conducive to infection, promotes and augments its severity, probably agitates and excites the tumor too much and carries a high mortality, particularly fulguration by the suprapubic method of approach. In at least 6 or 7 patients, the dose of radium seemed inadequate; when a large dose was used a somewhat better result was noted. Resection unless thoroughly performed does not offer an aid to treatment. The death rate is high, and the end-results are poor. A study of the cases of carcinoma disclosed the futility of fulguration alone. The group in which radium was used revealed a more noticeable effect on the tumor, longer periods of freedom from recurrence, greater span of life and practically no mortality. The patients who received the large doses of radium seemed to obtain the most satisfactory results.

Stones.—Higgins,[28] in his experiments, found that when animals were given a diet deficient in vitamin A for two hundred and fifty days necropsy revealed the presence of vesical calculi in 88 per cent and of renal calculi in 42 per cent. It likewise was shown that if vitamin A alone was added to the diet the formation of calculi was prevented. It has been stated that calculi have been produced experimentally only in white rats, a species remote phylogenetically from man. Therefore, a group of 7 dogs was maintained on a diet deficient in vitamin A for

27. Parmenter, F. J., and Leutenegger, C. J.: Bladder Tumors, J. Urol. **35**: 316-320 (March) 1936.

28. Higgins, C. C.: Further Observations on the Experimental Production of Urinary Calculi, Tr. Am. A. Genito-Urin. Surgeons **28**:157-162, 1935.

eleven months. Cystotomy was performed on 4 of these animals, under ether anesthesia. Multiple stones were found in the bladders of 3, and neither stone nor sand was noted in the fourth dog.

The possibility of producing calculi composed of uric acid and urates was then considered. The fact that birds eliminate uric acid and that the majority of the urea is converted into uric acid was well known. Therefore, observations were made on a group of chickens placed on a diet deficient in vitamin A. At necropsy, five months later, the kidneys were found to be somewhat pale and to contain urates and sand, and the ureters contained urates and small calculi of uric acid. Hard concretions of uric acid were present in the cloaca. In order to produce calculi similar to stones in the bladder, colostomy was performed on the chickens, thus diverting the fecal stream and utilizing the lower segment of the bowel and the cloaca as a bladder. From this structure, small calculi were easily removed for chemical examination, which revealed that they were composed purely of uric acid and urates.

Obstruction of the Neck of the Bladder.—Caulk [29] stated that the development and perfection of instruments of small caliber, the tolerance of infants and children to instrumentation when judiciously performed and the cooperation of the pediatrician in seeking special investigation of the urinary organs of children have tended to advance the urologic treatment of infants and young persons. Obstructions along the urinary tract are common and occur mainly at the normal physiologic constrictions, the ureteropelvic juncture, the intravesical ureter and the internal orifice of the bladder.

The clinical pictures resulting from obstructions in different portions of the urinary system may be similar, and the general physical signs may appear misleading. For practical purposes, and as an aid to the clinician, there are certain diagnostic procedures which may be helpful. The first is the determination of the total renal function by tests of elimination with drugs such as phenolsulfonphthalein or by tests of retention secured through a determination of the blood for its nitrogenous elements. The presence or absence of residual urine should be determined. If it is present, it usually indicates that the condition results from obstruction at the internal orifice of the bladder and is probably bilateral. The cystogram may afford information in revealing the topographic outline of the urinary system. Intravenous urography may be serviceable for delineating the outline of the urinary tract, but in Caulk's experience this method has not been entirely reliable. Cystoscopy is usually necessary before any definite plan of corrective therapy may be satisfactorily applied, and children tolerate this type of manipulation

29. Caulk, J. R.: Obstructions at the Bladder Neck in Infants and Children, Tr. Am. A. Genito-Urin. Surgeons **28**:287-296, 1935.

satisfactorily. Anesthesia was required in only 35 per cent of the cases. The importance of regurgitation of the contents of the bladder into the ureters and renal pelves cannot be overestimated.

Fourteen punch operations and 2 suprapubic operations were performed on 16 children because of obstruction at the neck of the bladder. Six operations were performed because of valves, 1 because of valve and bar, 7 because of contracture of the neck of the bladder and 2 because of lobules. The child's punch was used in 9 cases and the baby punch in 5. All of the children who had residual urine and gave evidence of urosepsis received preliminary treatment by drainage with an indwelling catheter, copious flushing of the bladder and urinary antiseptics, frequently by subcutaneous injections of saline solution and intravenous injection of solutions of dextrose and occasionally by transfusions, until their condition appeared sufficiently satisfactory for any type of operation.

The punch with its obturator was passed into the bladder, which had previously been filled with sterile water or a solution of boric acid. For infants the baby punch, no. 14 French, was used, and for larger children the child's punch, no. 18, was employed. After the introduction of the instrument, the obturator was removed, and the instrument gradually was withdrawn until the water ceased to flow. Previous cystoscopic examination had determined the exact nature of the obstruction. If it was a contracture of the neck of the bladder the slot of the instrument was brought out in the midline below. The eye-piece of the instrument was lightly elevated, the tube was evacuated and dried with a cotton pledget, and a working element carrying the cautery blade was passed through the sheath of the instrument until it engaged the obstruction. The current was then turned on, and by a rotary motion the obstructing band was removed with the punch. In cases of urethral valves, which are always lateral, the instrument was inserted in the same manner, but the slot of the instrument was pressed toward the side from which the operator expected to remove a central section from the band. In none of these patients operated on by the punch method was there any bleeding. A small indwelling catheter was left in place for twenty-four hours. There was no hemorrhage after operation, and in only 1 case was there any febrile reaction. These children tolerated such operations better than adults. No complications developed.

Results were excellent in 13 of the patients. Two patients were improved, and the results were not entirely satisfactory, but further surgical procedures were not authorized by the parents. One patient with pronounced spina bifida, with a thin, delicate valve, showed no improvement after removal of the valve.

Rupture.—Scholl [30] stated that the factors usually associated in producing rupture of the bladder are distention, a variable type of trauma and not infrequently an associated mental or alcoholic incompetence. Cases in which rupture of the bladder occurs in association with hypertrophy of the prostate gland are rare, but references to such conditions are occasionally noted in the literature. Rupture in such cases is primarily due to obstruction at the neck of the bladder and secondarily to increased intravesical pressure, plus degenerative changes in the wall of the bladder.

Scholl reported a case of rupture of the bladder resulting from distention of the organ, caused by prostatic obstruction. Patients with traumatic rupture of the bladder generally have severe pain in the lower part of the abdomen at the time of injury. This pain is continuous and associated with vesical tenesmus, and usually the patient is in moderate shock. The symptoms in cases of spontaneous rupture differ only slightly from those in cases in which rupture is caused by trauma. Spontaneous rupture of the bladder is more likely to occur among elderly patients with a history of involvement of the bladder of long standing.

The treatment in both the intraperitoneal and the extraperitoneal type of rupture is usually immediate operation. This condition is a surgical emergency, and delay, particularly when rupture into the peritoneal cavity has occurred, is as dangerous as in the case of any other acute abdominal lesion. When the tear has been through the peritoneum, the abdomen is opened, the bulk of the fluid is withdrawn by suction and the rent in the bladder is closed. Both the peritoneal cavity and the bladder are then adequately drained. In the extraperitoneal type of rupture the main procedure is drainage of the bladder, together with drainage of any perivesical pockets or areas of extravasation. Usually patients with rupture of the bladder are in poor general condition, and rapid, accurate operation is necessary. In the early days of surgery, almost all patients with rupture of the bladder died. The abdomen was not opened without the possibility of peritonitis occurring; consequently there are many patients who were not treated by operation. The associated lesions and complications took their toll, and rupture of the bladder was a serious condition. The present mortality, although still high, is mainly due to the tremendous shock and the coincidental lesions, conditions placing the patient beyond help when first seen. In only a small percentage of cases is the high mortality now due to delayed or unskilful procedures. In cases in which there are no complications, when operation is early the prognosis for both intraperitoneal and extraperitoneal rupture of the bladder should be favorable.

30. Scholl, A. J.: Rupture of the Urinary Bladder Associated with Prostatic Hypertrophy, J. A. M. A. **106**:701-704 (Feb. 29) 1936.

Syphilis.—Finestone [31] presented an analysis of 158 cases of syphilis of the bladder. There is a scarcity of data in the reported cases, which were neither thoroughly studied nor followed and adequately controlled. Only 8 investigators subjected the lesions to microscopic study. Only 1 investigator discovered the typical histopathologic picture of the disease. It was claimed that 2 investigators found specific histopathologic changes, but the cases were not reported in detail. The 5 other investigators gave descriptions of nonspecific inflammation. Two cases, 1 of which revealed all of the diagnostic criteria used in most of the cases, were described in detail; this demonstrates the pitfalls which are encountered in the presence of disease of the bladder and concomitant syphilis.

Disturbances of Innervation.—By means of an air-water manometer and recording tambour, Lewis, Langworthy and Dees [32] made graphic records of the behavior of the detrusor muscle during filling of the bladder. The muscle of the bladder characteristically responds to the stimuli of stretching, and significant information can be obtained by observing and recording waves of contraction of the bladder. Patients who had either bilateral or unilateral injuries of the pyramidal tract or had lesions of motor tracts in the spinal cord were studied. With release from cortical control, the "stretch reflex" is hyperactive. The bladder empties precipitously with a small volume of fluid. When the motor pathways from the midbrain are injured bilaterally along with the corticospinal tracts, the waves of contraction of the bladder are frequent but of small amplitude. They are ineffective in emptying the bladder. A study of contraction waves of the muscle during filling is of aid in forming an opinion of the efficiency of a bladder with injured innervation.

Langworthy and Dees [33] presented records of activity of the bladder in 4 cases of spina bifida. The neurologic involvement in each of the patients was of different degree. It is possible to distinguish predominant involvement of the posterior or sensory sacral roots from that of the anterior or motor roots. The importance of studying waves of vesical contraction is stressed. They may occur spontaneously and rhythmically or in response to sudden stretch of the muscle. If the waves are capable of summation into a strong, tetanic contraction, the bladder is emptied efficiently.

---

31. Finestone, E. O.: Syphilis of the Bladder, Surg., Gynec. & Obst. **62**: 93-113 (Jan.) 1936.

32. Lewis, L. G.; Langworthy, O. R., and Dees, J. E.: Bladder Abnormalities Due to Injury of Motor Pathways in the Nervous System, J. A. M. A. **105**:2126-2131 (Dec. 28) 1935.

33. Langworthy, O. R., and Dees, J. E.: A Study of Bladder Disturbances in Spina Bifida, J. Urol. **35**:213-226 (Feb.) 1936.

Closure of Incisions.—Davis [34] stated that quicker and more satisfactory healing of suprapubic incisions of the bladder may be obtained by diverting the drainage of urine from the main operative incision in the wall of the abdomen and by allowing the incision to heal by primary intention. The technic employed was a modification of the Pfannenstiel incision. The incision was made in the usual way, except that it was from 4 to 4.5 cm. above the upper border of the symphysis. This required care to avoid injuring the peritoneum but did not interfere with the exposure or incision of the bladder. A mushroom drain of any type desired may be sutured into the bladder. The bladder was then protected by a finger in the prevesical space, and a stab wound was made from the outside through the middle of either rectus muscle and half way between the incision and the symphysis. A large curved clamp was passed through this stab wound, and with it the drainage tube, a Dakin tube, and a cigaret drain were drawn out together through the wound. The incision was then tightly closed in layers. Suturing of the rectus muscles closed the incision completely from the prevesical space.

The sinuses produced by this method tend to contract rapidly, probably because they are closely surrounded by the tissue of the rectus muscles. For this reason leakage of urine around the tube was rare, and the fistula tended to close quickly after the tube was removed. The tube can be replaced if necessary, preferably with a Malecot drain. The original tube may be of any size, but the aforementioned characteristics of the fistula make this method of operating less desirable in cases in which extensive intravesical procedures may become necessary after operation. It is suitable, however, for cystostomy, lithotomy and other procedures involving less risk of hemorrhage.

Displacement.—Hepler [35] reported 5 cases of displacement of the bladder secondary to suppurative arthritis of the hip and osteomyelitis of the pelvic bones in children and described an operation for impending perforation.

This displacement is caused by the intrusion into the pelvis of an enormous involucrum. The bladder becomes attached to the involucrum and is displaced laterally. This displacement is caused not by an intrapelvic abscess, but by a hard bony mass. Perforation of the bladder is threatened or impending by sequestrums, with the production of an

34. Davis, D. M.: A New Method of Closing Suprapubic Bladder Incisions, with Remarks on the Prevention and Treatment of Infection in Urinary Wounds, J. Urol. **35**:41-48 (Jan.) 1936.

35. Hepler, A. B.: Bladder Displacement Secondary to Suppurative Arthritis of the Hip and Osteomyelitis of the Pelvic Bones in Children: Operation for Impending Perforation, J. Urol. **35**:32-40 (Jan.) 1936.

osteovesical fistula. When perforation occurs it is chronic or subacute, with the entire side of the bladder firmly adherent to the involucrum, so that there is no urinary extravasation or leakage.

This condition has not been described before, possibly because of the absence of signs and symptoms referable to the urinary tract. Even in the 2 cases in which perforation was present, there were no subjective symptoms and an examination was made simply because of a persistent pyuria.

The absence of urinary signs or symptoms is no indication that displacement of the bladder is not present. Therefore, cystograms should be made as a routine measure.

If displacement is present, then the operation described should be performed, first to prevent perforation of the bladder, and second, of equal importance, to bring about a more rapid subsidence of the osteomyelitis by sequestrectomy, curettage and drainage of the sinuses through the pelvis. After months of the usual orthopedic treatment, the 3 patients on whom operation was performed improved rapidly and were discharged in a comparatively short time.

Once corrected, this condition does not tend to recur provided the osteomyelitic region is adequately drained.

(To be concluded.)

INDEX TO VOLUME 33

Abdomen: See also Gastro-Intestinal Tract; Pelvis
allergy as explanation of dehiscence of wound and incisional hernia, 197
cutaneous hyperalgesia; experimental study, 108

Abnormalities and Deformities: See also under names of organs and regions, as Fibula; Foot, deformities; Kidneys, anomalies; Ureters; etc.
genetics of congenital deformities, 897

Abscess: See under names of organs and regions, as Kidneys, abscess; Lungs, abscess; etc.

Acetabulum: See also Hip Joint
etiology of deep acetabulum and intrapelvic protrusion, 122
tuberculosis of, 899

Acetylcholine: See Choline and Choline Derivatives

Acromioclavicular Joint: See under Shoulder

Actinomycosis of kidneys, 324

Adenoma, arrhenoblastoma of ovary; testicular adenoma tubulare, 392
hypoparathyroidism following operation for hyperparathyroidism due to adenoma tolerance for parathyroid extract, 808

Adrenals, adrenogenital syndrome, 1104
tumor, 1105
tumor of kidney or adrenal gland, 980

Allergy: See Anaphylaxis and Allergy

Amputation, election of site in diabetic gangrene, 906
of lower third of thigh, new, 180

Anaphylaxis and Allergy; allergy as explanation of dehiscence of wound and incisional hernia, 197

Anastomoses: See under Blood, vessels

Anemia, sickle cell, changes in bone in, 898

Anesthesia, spinal; experimental basis of some prevailing clinical practices, 825

Aneurysms of hand, 267

Angioma, vertebral, 901

Ankle: See also Astragalus; Foot
malunited fractures affecting ankle joint, 184

Ankylosis: See Joints; Spine

Anomalies: See Abnormalities and Deformities; and under names of organs and regions

Antrum, malignant tumor of antrum or superior maxilla, 968

Arms: See Forearm; Humerus; Radius

Arrhenoblastoma of ovary; testicular adenoma tubulare, 392

Arteries: See also Aneurysms; Blood, pressure; Blood, vessels; Embolism; Pulse; Thrombosis; etc.
congenital abnormal arteriovenous anastomoses of extremities with reference to diagnosis by arteriography and by oxygen saturation test, 848
femoral; traumatic arteriovenous fistula involving right femoral artery and vein; spontaneous closure, 248

Arthritis and injuries to joints, 213
arthroplasty in ankylosis following gonorrheal arthritis, 907
atrophic and hypertrophic, protein studies in, 901
chronic, roentgen aspects, 901
chronic, synovectomy of knee joint in, 907

Arthritis—Continued
degenerative type, experimental and pathologic studies, 173
of hip, displacement of bladder in, 1115

Astragalus, fracture; injury of persons who fly gliders, 184

Athletics, dislocation of head of fibula in sports, 910

Aviation, fracture of astragalus; injury of persons who fly gliders, 184

Avitaminosis: See under Vitamins

Bacteria: See Streptococci; etc.

Barr, J. S.: Sixtieth report of progress in orthopedic surgery, 168
Sixty-first report of progress in orthopedic surgery, 895

Baxter, N. E.: Duodenogastric intussusception; experimental study of peptic ulcer, 1

Beck, W. C.: Preparation of operative field; report of survey of 17 surgical teaching clinics, 876

Behrend, M.: Arrhenoblastoma of ovary; testicular adenoma tubulare, 392

Bennett, G. E.: Cysts of semilunar cartilages, 92

Berman, J. K.: Duodenogastric intussusception; experimental study of peptic ulcer, 1

Bile, acids, differential analysis in human gallbladder bile, 913
peritonitis, lethal factors in; "surgical shock," 576

Bile Ducts: See also Gallbladder
endocholedochal section of sphincter of Oddi, 696

Bilharziasis: See Schistosomiasis

Bisgard, J. D.: Ossification; influence of mineral constituents of bone, 926

Bissell, A. D.: Estrus cycles in mice of cancerous and noncancerous strains, 515

Bladder: See also Urinary Tract
closure of incisions, 1115
cystectomy, 342
displacement, 1115
disturbances of innervation, 1114
exstrophy in relation to locomotor function, 897
nerve control, 347
obstruction of neck of bladder, 1111
resection, 345
rupture, 1113
Sphincter: See Sphincter muscles
syphilis, 1114
tuberculosis, 343
tumors, 339, 1105
tumors; benign or malignant tumor of urinary bladder, 980

Blood: See also Anemia; Leukemia
circulation; effects of circulatory disturbances on structure and healing of bone; injuries of head of femur in young rabbits, 225
pressure, mechanical decompression of intestine in treatment of ileus; effect of stripping on blood pressure, 664
proteins; protein studies in atrophic and hypertrophic arthritis, 901
vessels, congenital abnormal arteriovenous anastomoses of extremities with reference to diagnosis by arteriography and by oxygen saturation test, 848

Bones: See also under names of bones
analysis of living patients with primary malignant tumor of bones, 174
cancer; chronic osteomyelitis associated with malignant changes, 171
changes in leukemia in children, 898
changes in sickle cell anemia, 898
Diseases: See Osteitis; Osteochondritis; Osteomyelitis; etc.
effects of circulatory disturbances on structure and healing of bone; injuries of head of femur in young rabbits, 225
fragility; brittle bones and blue scleras, 178
growth; arrest of growth after fractures into epiphyses, 911
growth; effect of large doses of roentgen rays on growth of young bones, 186
Hodgkin's disease of, 902
osseous metastases with carcinoma of stomach, 175
ossification; influence of mineral constituents of bone, 926
tuberculosis of shafts of long bones, 172
tumors; unusual cartilaginous tumor formation of skeleton, 1054

Brain injuries, acute; analysis of temperature, pulse and respiration curves, 560

Breast, cancer, 990
cancer; estrus cycles in mice of cancerous and noncancerous strains, 515
cancer; roentgen irradiation of ovaries as supplement to surgical and radium therapy for mammary cancer, 554
idiopathic hypertrophy, surgical treatment, 253

Bronchi, experimental pulmonary abscess; transmission of disease to dogs by bronchial route, 649

Brunschwig, A.: Estrus cycles in mice of cancerous and noncancerous strains, 515

Calcaneum, therapy for fracture of os calcis, 184

Calculus: See Kidneys, calculi; Ureter, calculi; Urinary Tract, calculi; etc.

Callus: See also under Fractures
influence of motion on healing of fractures, 83

Cancer: See also Adenoma; Sarcoma; and under names of organs and regions, as Bones, cancer; Breast, cancer; Colon, cancer; Esophagus, cancer; Penis, cancer; Prostate, cancer; Stomach, cancer; Uterus, cancer; etc.
plan for treatment with small quantities of radium, 940

Carbuncle, Renal: See Nephritis

Carcinoma: See Cancer

Carpus: See Wrist

Cartilage: See also Joints; Osteochondritis; Ribs; etc.
unusual cartilaginous tumor formation of skeleton, 1054

Catheters, hydrodynamics of relief of distention in gastro-intestinal tract by suction applied to inlying catheters, 995

Cave, E. F.: Sixtieth report of progress in orthopedic surgery, 168
Sixty-first report of progress in orthopedic surgery, 895

Cervix: See under Uterus

Choline and Choline Derivatives, effect of acetylcholine and of physostigmine on gastro-intestinal motility; observations of normal animals and of animals with experimental peritonitis, 187

Chondrogenesis: See under Cartilage

Cleft Palate: See Palate

Clubfoot: See Foot, deformities

Colles Fracture: See Radius, fracture

Colloids, rôle of reticulo-endothelial system in deposition of colloidal and particulate matter in articular cavities, 68

Colon: See also Gastro-Intestinal Tract; Intestines
carcinoma of, 977

Colp, R.: Differential analysis of bile acids in human gallbladder bile, 913
Endocholedochal section of sphincter of Oddi, 696

Contracture, Dupuytren's, of fingers, 178
ischemic, 902
ischemic; Volkmann's contracture, 903
ischemic; Volkmann's ischemic paralysis, 176

Conway, J. H.: Leiomyoma of stomach, 792

CoTui: Spinal anesthesia; experimental basis of some prevailing clinical practices, 825

Cranium, cranial venous sinuses; correlation between skull markings and roentgenograms of occipital bone, 867
variations of cranial venous sinuses in region of torcular Herophili, 297

Cryptorchidism: See Testicles, undescended

Cuneiform Bone: See Tarsus

Cutler, E. C.: Neurofibroma and neurofibrosarcoma of peripheral nerves unassociated with Recklinghausen's disease; report of 25 cases, 733

Cystectomy: See under Bladder

Cysts: See under names of organs and regions, as Kidneys, cysts; Knee, cysts; Scrotum, cysts; Semilunar Cartilages, cysts; etc.

Dandy, W. E.: Operative experience in cases of pineal tumor, 19

David, V. C.: Aneurysms of hand, 267

Death, lethal factors in bile peritonitis; "surgical shock," 576

Deformities: See Abnormalities and Deformities; and under names of organs and regions

Degeneration, fatty; replacement lipomatosis, 332

Diabetes Mellitus, election of site of amputation in diabetic gangrene, 906

Doubilet, H.: Differential analysis of bile acids in human gallbladder bile, 913
Endocholedochal section of sphincter of Oddi, 696

Douglas, E.: Sarcoma of stomach, 467

Drainage, hydrodynamics of relief of distention in gastro-intestinal tract by suction applied to inlying catheters, 995

Dry, T. J.: Traumatic arteriovenous fistula involving right femoral artery and vein; spontaneous closure, 248

Duodenum, duodenogastric intussusception; experimental study of peptic ulcer, 1
Ulcers: See Peptic Ulcers

Dupuytren Contracture: See Contracture

Dura mater, variations of cranial venous sinuses in region of torcular Herophili, 297

Elbow, end-results of excision of, 907

Embolism, fat; experimental study on value of roentgenograms of chest in diagnosis, 708

Enuresis: See Urination, incontinence

Epiphyses, arrest of growth after fractures into epiphyses, 911

Epithelioma of penis, 982
of skin, 957

Ergosterol, irradiated; viosterol in prevention and treatment of rickets, tetany and allied diseases, 6 years' experience, 897

Esophagus, cancer of, 975

Estruation, estrus cycles in mice of cancerous and noncancerous strains, 515

Ethylene glycol and magnesium sulfate paste in treatment of inflammatory processes, 210

Extension, "well leg traction" in correcting orthopedic deformities, 904

Fat, effect of fat introduced into jejunum by fistula on motility and emptying time of stomach, 451

Femur: See also Hip Joint
congenital defects of femur, fibula and tibia, 349
effects of circulatory disturbances on structure and healing of bone; injuries of head of femur in young rabbits, 225
end-results of leg lengthening, 907
fractures of neck of femur, 910
fractures; survey of management of intracapsular fractures of neck of femur, 183
fractures, united, of neck of femur, 909

Fibrosarcoma of soft parts with reference to recurrence and metastasis, 425

Fibula, congenital defects of femur, fibula and tibia, 349
dislocation of head of fibula in sports, 910

Fingers and Toes, Contracture: See under Contracture
radical operation for hallux valgus, 180

Fistula, 347
arteriovenous, traumatic, involving right femoral artery and vein; spontaneous closure, 248
congenital abnormal arteriovenous anastomoses of extremities with reference to diagnosis by arteriography and by oxygen saturation test, 848
effect of fat introduced into jejunum by fistula on motility and emptying time of stomach, 451

Flatfoot: See Foot, flat

Flatulence, gaseous distention associated with mechanical obstruction of intestine, 146

Fomon, S.: Surgical treatment of idiopathic hypertrophy of breast, 253

Foot: See also Ankle; Astragalus; Calcaneum; Fingers and Toes; Metatarsus; etc.
deformities; arthrodesis of foot, 908
deformities; congenital supination deformity of forefoot, 168
deformities; tarsal ossification in patients with congenital clubfoot, 896
deformities; treatment of congenital clubfoot, 169
flat; congenital flatfoot, 168
march foot associated with undescribed changes in internal cuneiform and metatarsal bones, 175
treatment of tuberculosis of bones of feet, 900

Forearm, traumatic arterial thrombosis of, 905

Fractures: See also under names of bones, as Femur, fractures; Humerus, fractures; Metatarsus, fractures; Spine, fractures; etc.
callus formation in presence of foreign bodies, 911
Colles: See Radius, fracture
influence of motion on healing, 83
influence of roentgen irradiation on rate of healing, 186
sclerosing osteomyelitis following, 900

Frank, R.: Effect of acetylcholine and of physostigmine on gastro-intestinal motility; observations of normal animals and of animals with experimental peritonitis, 187

Freiberg, J. A.: Sixtieth report of progress in orthopedic surgery, 168
Sixty-first report of progress in orthopedic surgery, 895

Freund, E.: Congenital defects of femur, fibula and tibia, 349
Diffuse genuine phlebectasia; report of case, 113
Unusual cartilaginous tumor formation of skeleton, 1054

Gallbladder: See also Bile
differential analysis of bile acids in human gallbladder bile, 913

Gastro-Intestinal Tract: See also Colon; Intestines; Rectum; Stomach; etc.
effect of posterior pituitary extracts on motility of, 780
hydrodynamics of relief of distention by suction applied to inlying catheters, 995

Gastroscopy: See under Stomach

Gerber, I. E.: Endocholedochal section of sphincter of Oddi, 696

Glenn, F.: Sarcoma of stomach, 467

Globulin in Blood: See Blood, proteins

Glycosuria: See Urine, sugar

Goldman, A.: Experimental pulmonary abscess; transmission of disease to dogs by bronchial route, 649

Gonorrhea, arthroplasty in ankylosis following gonorrheal arthritis, 907

Gross, R. E.: Neurofibroma and neurofibrosarcoma of peripheral nerves unassociated with Recklinghausen's disease; report of 25 cases, 733

Gruskin Test: See Stomach, cancer

Gutierrez, R.: Review of urologic surgery, 315, 521, 1078

Hallux: See Fingers and Toes

Hand, aneurysms of, 267

Harkins, H. N.: Lethal factors in bile peritonitis; "surgical shock," 576

Harmon, P. H.: Lethal factors in bile peritonitis; "surgical shock," 576

Head: See Cranium

Hemangioma of voluntary muscle, 175
traumatic hemangiomatous tumors of skeletal muscle, 175

Hematuria, essential, 541

Hepler, A. B.: Review of urologic surgery, 315, 521, 1078

Hernia, allergy as explanation of dehiscence of wound and incisional hernia, 197
into umbilical cord and related anomalies, 1021

Hibbard, J. S.: Gaseous distention associated with mechanical obstruction of intestine, 146

Hinman, F.: Review of urologic surgery, 315, 521, 1078

Hinton, J. W.: Allergy as explanation of dehiscence of wound and incisional hernia, 197
Ethylene glycol and magnesium sulfate paste in treatment of inflammatory processes, 210

Hip Joint: See also Femur
dislocation, congenital; results of treatment, 169, 170
stabilization by transplantation of anterior muscles of thigh, 179

Hodgkin's Disease: See Lymphogranuloma

Horton, B. T.: Traumatic arteriovenous fistula involving right femoral artery and vein; spontaneous closure, 248

Horwitz, M. T.: Investigation into wiring of spinous processes as means of internal spinal fixation, 630

Hudson, J.: Lethal factors in bile peritonitis; "surgical shock," 576

Humerus, fractures; nailing of fractures of humeral head, 182
fractures of lateral condyle of, 909
Volkmann's contracture, 903

Hydronephrosis, 326, 1097
pseudohydronephrosis, 328

Hyperalgesia: See Hyperesthesia

Hyperesthesia; cutaneous hyperalgesia of abdomen, experimental study, 108

Hyperparathyroidism: See under Parathyroid

Hypoparathyroidism: See under Parathyroid

Hypospadias, 528

Ileus: See Intestines, obstruction
Industrial diseases, articular lesions following work with compressed air tools, 904
Infection: See under names of bacteria, as Streptococci; etc.
Inflammation, ethylene glycol and magnesium sulfate paste in treatment of inflammatory processes, 210
Intervertebral Disks: See Spine
Intestines: See also Colon; Duodenum; Gastro-Intestinal Tract; Rectum
effect of acetylcholine and of physostigmine on gastro-intestinal motility; observations of normal animals and of animals with experimental peritonitis, 187
obstruction; gaseous distention associated with mechanical obstruction of intestine, 146
obstruction; mechanical decompression in treatment of ileus; effect of intestinal activity, 670
obstruction; mechanical decompression in treatment of ileus; effect of stripping on blood pressure, 664
obstruction produced by mesenteric bands in association with failure of intestinal rotation, 47
studies in gastro-intestinal motility, 276

Jejunum: See under Fistula; Intestines
Ulcers: See Peptic Ulcers
Jirka, F. J.: Fat embolism; experimental study on value of roentgenograms of chest in diagnosis, 708
Joints: See also under names of individual joints, as Elbow; Hip Joint; etc.
arthroplasty in ankylosis following gonorrheal arthritis, 907
articular lesions following work with compressed air tools, 904
effect of immobilization on normal joint, 912
injuries, and arthritis, 213
Loose Bodies in: See also Osteochondritis dissecans; and under names of joints
loose bodies in, 178
osteochondritis dissecans as related to trauma, 903
rôle of reticulo-endothelial system in deposition of colloidal and particulate matter in articular cavities, 68
thermotherapy for articular disease, 912
Joplin, R. J.: Sixtieth report of progress in orthopedic surgery, 168
Sixty-first report of progress in orthopedic surgery, 895

Kidneys: See also Hydronephrosis; Urinary Tract
abscess, perinephric, 333
actinomycosis, 324
anomalies, 315, 1078
attempts to produce Paget's disease by pituitary and parathyroid extracts, 911
calculus, 321, 1088
cysts, 1095
extravasation from pelvis, 330
hydronephrosis, 1097
lymphatics, 1099
nephrectomy, transabdominal, 334
nephrotomy, 334
nephro-ureterectomy, 1102
perirenal lipomatosis, 1101
polycystic diseases, 331
ptosis, 1082
replacement lipomatosis, 332
schistosomiasis, 1093
trauma, 328
tuberculosis, 323, 1092
tumors, 317, 1085
tumors of kidney or adrenal gland, 980
Kistler, G. H.: Effect of circulatory disturbances on structure and healing of bone; injuries of head of femur in young rabbits, 225
Kling, D. H.: Arthritis and injuries to joints, 213
Knee: See also Patella; Semilunar Cartilages
cysts, tuberculous, 898
innervation of skin of anterior aspect of knee, 177
roentgenograms on curved cassette to show loose bodies in knee joint, 176
synovectomy in chronic arthritis, 907
Kuhns, J. G.: Rôle of reticulo-endothelial system in deposition of colloidal and particulate matter in articular cavities, 68
Sixtieth report of progress in orthopedic surgery, 168
Sixty-first report of progress in orthopedic surgery, 895
Kurtz, A. D.: Investigation into wiring of spinous processes as means of internal spinal fixation, 630

Larynx, carcinoma of, 970
Leiomyoma of stomach, 792
Leukemia, changes in bone in children, 898
Levine, S.: Arrhenoblastoma of ovary; testicular adenoma tubulare, 392
von Lichtenberg, A.: Review of urologic surgery, 1078
Lipoma, perirenal lipomatosis, 1101
Lipomatosis: See Degeneration, fatty
Lips, cancer of, 961
quantitative studies on congenital clefts of lip, 1046
Locomotion, exstrophy of bladder in relation to locomotor function, 897
Lungs, abscess, experimental; transmission of disease to dogs by bronchial route, 649
Lymph Nodes, cancer, metastatic, in cervical lymph nodes, 973
Lymphatic System, lymphatics of kidney, 1099
Lymphogranuloma, Hodgkin's disease of bone, 902

McClintock, J. C.: Lesions of thyroglossal tract, 890
McClure, R. D.: Hypoparathyroidism following operation for hyperparathyroidism due to adenoma tolerance for parathyroid extract, 808
McCord, W. M.: Congenital abnormal arteriovenous anastomoses of extremities with reference to diagnosis by arteriography and by oxygen saturation test, 848
Magnesium sulfate paste and ethylene glycol in treatment of inflammatory processes, 210
Mahorner, H. R.: New test for evaluating circulation in venous system of lower extremity affected by varicosities, 479
Mammary Gland: See Breast
March Foot: See Foot
Maskin, M.: Effect of posterior pituitary extracts on motility of gastro-intestinal tract, 780
Mayo, C. W.: Intestinal obstruction produced by mesenteric bands in association with failure of intestinal rotation, 47
Melanoma, malignant, 960
Meniscus: See Semilunar Cartilages
Mesentery, intestinal obstruction produced by mesenteric bands in association with failure of intestinal rotation, 47
Metacarpus, dislocation of base of fifth metacarpal bone, 910
Metals, rusting of tissues with rustless nails and wires, 179

Metatarsus: See also Foot
fractures; ligaments of arch of foot and mechanism of metatarsal fractures, 185
march foot associated with undescribed changes in internal cuneiform and metatarsal bones, 175
therapy of aseptic necrosis, 905

Milgram, J. E.: Sixtieth report of progress in orthopedic surgery, 168
Sixty-first report of progress in orthopedic surgery, 895

Minerals, ossification; influence of mineral constituents of bone, 926

Movements, influence of motion on healing of fractures, 83
of wrist joint, 178

Mulinos, M. G.: Studies in gastro-intestinal motility, 276

Muscles, blood flow through skeletal muscle in relation to its contraction, 185
influence of motion on healing of fractures, 83
regeneration of muscular fibers after injury, 905
rupture of long head of biceps brachialis muscle, 906
skeletal, traumatic hemangiomatous tumors of, 175
stabilization of hip by transplantation of anterior muscles of thigh, 179
voluntary, hemangioma of, 175

Necheles, H.: Effect of acetylcholine and of physostigmine on gastro-intestinal motility; observations of normal animals and of animals with experimental peritonitis, 187
Effect of posterior pituitary extracts on motility of gastro-intestinal tract, 780

Nephrectomy; Nephrotomy: See under Kidneys

Nephritis, renal carbuncle, 325

Nerves, neurofibroma and neurofibrosarcoma of peripheral nerves unassociated with Recklinghausen's disease; report of 25 cases, 733

Nervous System, disturbances of innervation, 1114
neurogenic sarcoma, 961

Neuritis, traumatic arterial thrombosis of forearm, 905

Neurofibroma and neurofibrosarcoma of peripheral nerves unassociated with Recklinghausen's disease; report of 25 cases, 733

Neurofibrosarcoma and neurofibroma of peripheral nerves unassociated with Recklinghausen's disease; report of 25 cases, 733

Nixon, S.: Cutaneous hyperalgesia of abdomen; experimental study, 108

Occipital bone, cranial venous sinuses; correlation between skull markings and roentgenograms of occipital bone, 867

Occupational Diseases: See Industrial diseases

Ochsner, A.: Mechanical decompression of intestine in treatment of ileus; effect of intestinal activity, 670
Mechanical decompression of intestine in treatment of ileus; effect of stripping on blood pressure, 664
New test for evaluating circulation in venous system of lower extremity affected by varicosities, 479

O'Conor, V. J.: Review of urologic surgery, 315, 521, 1078

Oddi's Sphincter: See Sphincter Muscles

Orthopedic surgery, sixtieth report of progress in, 168
sixty-first report of progress in, 895

Ossification, influence of mineral constituents of bone, 926

Osteitis deformans, attempts to produce Paget's disease by pituitary and parathyroid extracts, 911

Osteochondritis deformans juvenilis, histopathologic study in case of Perthes' disease of traumatic origin, 609
dissecans as related to trauma, 903

Osteogenesis: See Bones, growth

Osteomyelitis, acute and chronic, in child, 170
chronic, associated with malignant changes, 171
displacement of bladder in, 1115
sclerosing, following fractures, 900

Osteoporosis: See Bones, fragility

Ovary, arrhenoblastoma; testicular adenoma tubulare, 392
malignant tumor, 990
roentgen irradiation of ovaries as supplement to surgical and radium therapy for mammary cancer, 554

Oxygen, congenital abnormal arteriovenous anastomoses of extremities with reference to diagnosis by arteriography and by oxygen saturation test, 848

Pack, G. T.: Plan for treatment of cancer with small quantities of radium, 940

Paget's Disease of Bones: See Osteitis deformans

Paine, J. R.: Hydrodynamics of relief of distention in gastro-intestinal tract by suction applied to inlying catheters, 995

Palate, quantitative studies on congenital clefts of lip, 1046

Paralysis: See also Poliomyelitis
spastic child, 903
Volkmann's: See Contracture, ischemic

Parathyroid, attempts to produce Paget's disease by pituitary and parathyroid extracts, 911
hypoparathyroidism following operation for hyperparathyroidism due to adenoma tolerance for parathyroid extract, 808

Parotid gland, tumor of, 973

Patella: See also Knee
fractures of, 910
operative treatment of habitual dislocation, 179

Pelvis, osteomyelitis, displacement of bladder in, 1115

Penis, carcinoma, 527
epithelioma of, 982

Peptic Ulcers, experimental study; duodenogastric intussusception, 1

Peritonitis, effect of acetylcholine and of physostigmine on gastro-intestinal motility; observations of normal animals and of animals with experimental peritonitis, 187
lethal factors in bile peritonitis; "surgical shock," 576
streptococcic, primary, 714

Perthes' Disease: See Osteochondritis deformans juvenilis

Peyton, W. T.: Quantitative studies on congenital clefts of lip, 1046

Phlebectasia: See Veins, dilatation

Phosphatase, influence of roentgen irradiation on rate of healing of fractures, 186

Physostigmine, effect of acetylcholine and of physostigmine on gastro-intestinal motility; observations of normal animals and of animals with experimental peritonitis, 187

Pich, G.: Histopathologic study in case of Perthes' disease of traumatic origin, 609

Pineal body, tumor, operative experience in, 19

Pituitary Preparations, attempts to produce Paget's disease by pituitary and parathyroid extracts, 911
effect of posterior pituitary extracts on motility of gastro-intestinal tract, 780

Poliomyelitis, 171
posterior bone block of ankle joint, 908
seventh nerve as pathway for transmission of virus, 900
Pollock, L. H.: Primary streptococci peritonitis, 714
Portal vein, chronic occlusion, 397
Potts, W. J.: Influence of motion on healing of fractures, 83
Pratt, G. H.: Diagnosis of cancer of stomach; use of gastroscope and Gruskin test, 138
Prepuce: See Penis
Priestley, J. T.: Review of urologic surgery, 315, 521, 1078
Prostate, carcinoma of, 981
hemorrhage, 522
hypertrophy, 521
resection, 522
Pulse, acute cerebral injuries; analysis of temperature, pulse and respiration curves, 560
Pyuria: See Urinary Tract, infections

Rachitis: See Rickets
Radium, plan for treatment of cancer with small quantities of radium, 940
Radius, fracture of base of radius in adults, 182
fracture; treatment of Colles' fracture, 183
Raiford, T. S.: Studies in gastro-intestinal motility, 276
Rechtman, A. M.: Etiology of deep acetabulum and intrapelvic protrusion, 122
Rectum, carcinoma of, 978
Respiration, acute cerebral injuries; analysis of temperature, pulse and respiration curves, 560
Reticulo-endothelial system, rôle in deposition of colloidal and particulate matter in articular cavities, 68
Rheumatic fever, studies relating vitamin C deficiency to rheumatic fever and rheumatoid arthritis, 172
Ribs, tuberculosis of rib cartilage, 899
Rickets, viosterol in prevention and treatment of rickets, tetany and allied diseases, 6 years' experience, 897
Ritchie, H. P.: Quantitative studies on congenital clefts of lip, 1046
Roberts, S. M.: Sixtieth report of progress in orthopedic surgery, 168
Sixty-first report of progress in orthopedic surgery, 895
Roentgen Rays, effect of large doses on growth of young bones, 186
influence of roentgen irradiation on rate of healing of fractures, 186
Therapy: See under names of organs, regions and diseases

Sarcoma, neurogenic, 961
of stomach, 467
Scaphoid Bone, fracture of carpal scaphoid, 183
tarsal; therapy of aseptic necrosis, 905
Scapula, fracture, mechanism of, 181
treatment of congenital elevation of, 895
Schistosomiasis of kidney, 1093
Scholl, A. J.: Review of urologic surgery, 315, 521, 1078
Scleras, blue, and brittle bones, 178
Scrotum, cysts, and congenital canals, 539
Scuderi, C. S.: Fat embolism; experimental study on value of roentgenograms of chest in diagnosis, 708
Seeds, A. E.: Cranial venous sinuses; correlation between skull markings and roentgenograms of occipital bone, 867
Semilunar Bone, therapy of aseptic necrosis, 905
anatomic observations on development of necrosis of carpal semilunar bone, 185
Semilunar Cartilages, cysts of, 92
injuries, 177
Shaw, M. B.: Cysts of semilunar cartilages, 92
Shevky, M. C.: Experimental pulmonary abscess; transmission of disease to dogs by bronchial route, 649
Shock, surgical; lethal factors in bile peritonitis, 576
Shoulder: See also Humerus; Scapula
late results of dislocation of upper extremity and its prevention, 181
roentgenologic study of acromial arthritis, 173
stabilization of acromioclavicular joint, 179
Simonds, J. P.: Chronic occlusion of portal vein, 397
Skin, epithelioma of, 957
innervation, of anterior aspect of knee, 177
Skull: See Cranium
Smelo, L. S.: Problem of wound healing; effect of local agents, 493
Sommer, G. N. J., Jr.: Fibrosarcoma of soft parts with reference to recurrence and metastasis, 425
Spermatic cord, division, 537
torsion, 539
Sphincter muscles, endocholedochal section of sphincter of Oddi, 696
Spine, angioma, vertebral, 901
avulsions of spinous processes, 181
changes in development in vertebral articular facets, 174
fracture, local anesthesia for, 180
fractures, compression, 909
intervertebral disk, 174
investigation into wiring of spinous processes as means of internal spinal fixation, 630
spondylitis ankylopoietica, 901
Spondylitis: See under Spine
Sports: See Athletics
Stirling, R. I.: Sixtieth report of progress in orthopedic surgery, 168
Sixty-first report of progress in orthopedic surgery, 895
Stomach: See also Gastro-Intestinal Tract
cancer, 976
cancer, and osseous metastases, 175
cancer, diagnosis; use of gastroscope and Gruskin test, 138
duodenogastric intussusception; experimental study of peptic ulcer, 1
effect of fat introduced into jejunum by fistula on motility and emptying time of stomach, 451
leiomyoma of, 792
sarcoma of, 467
Ulcers: See Peptic Ulcers
Storck, A. H.: Mechanical decompression of intestine in treatment of ileus; effect of intestinal activity, 670
Mechanical decompression of intestine in treatment of ileus; effect of stripping on blood pressure, 664
Strauss, A. A.: Effect of posterior pituitary extracts on motility of gastro-intestinal tract, 780
Strauss, S.: Effect of posterior pituitary extracts on motility of gastro-intestinal tract, 780

Streptococci, primary streptococcic peritonitis, 714
Suction: See under Drainage
Suprarenals: See Adrenals
Surgery, preparation of operative field; report of survey of 17 surgical teaching clinics, 876
Symphysis pubis, tuberculosis of, 172
Synosteosis, radio-ulnar, 896
Synovial membrane, synovectomy of knee joint in chronic arthritis, 907
Syphilis: See also under names of organs and regions, as Bladder, syphilis; etc.
infantile congenital, with positive roentgen but negative serologic findings, 171
Syringomyelia, surgical treatment of, 908

Taft, E.: Effect of posterior pituitary extracts on motility of gastro-intestinal tract, 780
Talus: See Astragalus
Tarsus, march foot associated with undescribed changes in internal cuneiform and metatarsal bones, 175
Temperature, acute cerebral injuries; analysis of temperature, pulse and respiration curves, 560
thermotherapy for articular disease, 912
Tendons, tensile strength of human tendons, 911
traumatic arterial thrombosis of forearm, 905
Teratoma of testis, 983
Testicles, arrhenoblastoma of ovary; testicular adenoma tubulare, 392
teratoma of, 983
tumors, 532
undescended, 535
Tetany, viosterol in prevention and treatment of rickets, tetany and allied diseases, 6 years' experience, 897
Thermotherapy for articular disease, 912
Thompson, G. J.: Review of urologic surgery, 315, 521, 1078
Thorax, fat embolism; experimental study on value of roentgenograms of chest in diagnosis, 708
Thrombophlebitis migrans, 177
Thrombosis, sinus; variations of cranial venous sinuses in region of torcular Herophili, 297
traumatic arterial thrombosis of forearm, 905
Thunig, L. A.: Hernia into umbilical cord and related anomalies, 1021
Thyroglossal tract, lesions of, 890
Thyroid diseases; chronic thyroiditis; comparative analysis of 100 cases, 545
Thyroiditis: See Thyroid, diseases
Tibia, congenital defects of femur, fibula and tibia, 349
derotation of, 908
end-results of leg lengthening, 907
Tissues, rusting with rustless nails and wires, 179
Toes: See Fingers and Toes
Tongue, cancer, 962
Tonsil, malignant tumor of, 966
Torcular: See Dura mater
Trauma, histopathologic study in case of Perthes' disease of traumatic origin, 609
Trochanter: See Femur
Tuberculosis: See Acetabulum tuberculosis; Bladder, tuberculosis; Bones, tuberculosis; Kidneys, tuberculosis; Spine, tuberculosis; etc.
Tumors: See Adenoma; Angioma; Cholesteatoma; Epithelioma; Melanoma; Sarcoma; Teratoma; etc.; and under names of organs and regions as Bladder, tumors; Bones, tumors; Kidneys, tumors; etc.
Ulcers, Peptic: See Peptic Ulcers
Umbilical cord, hernia into umbilical cord and related anomalies, 1021
Ureterocele: See Ureters, dilatation
Ureters: See also Urinary Tract
anomalies, 337
calculus, 335
dilatation, 339
dilatation; ureterocele, 337
diversion of urinary stream, 539
nephro-ureterectomy, 1102
obstruction, 336
Urethra, injuries, 530
stricture, 531
Urinary Tract: See also Kidneys; Ureters; etc.
calculi, 1110
infections; pyuria, 543
Urination, incontinence, 346
Urine, sugar; renal glycosuria, 1098
Urolithiasis: See Urinary Tract, calculi
Urologic surgery, review of, 315, 521, 1078
Uterus, cancer of body of uterus, 989
carcinoma of cervix, 984

Varicose veins, new test for evaluating circulation in venous system of lower extremity affected by varicosities, 479
Veal, J. R.: Congenital abnormal arteriovenous anastomoses of extremities with reference to diagnosis by arteriography and by oxygen saturation test, 848
Veins: See also Embolism; Thrombosis; etc.
congenital abnormal arteriovenous anastomoses of extremities with reference to diagnosis by arteriography and by oxygen saturation test, 848
dilatation; diffuse genuine phlebectasia; report of case, 113
femoral; traumatic arteriovenous fistula involving right femoral artery and vein; spontaneous closure, 248
new test for evaluating circulation in venous system of lower extremity affected by varicosities, 479
variations of cranial venous sinuses in region of torcular Herophili, 297
Varicose: See Varicose veins
Verbrugge, J.: Review of urologic surgery, 315, 521
Vertebra: See Spine
Viosterol: See Ergosterol, irradiated
Virilism, adrenogenital syndrome, 1104
Vitamin A deficiency, urinary stones due to, 1110
C, studies relating vitamin C deficiency to rheumatic fever and rheumatoid arthritis, 172
Volkmann Contracture: See Contracture, ischemic
Vulva, malignant tumors of, 984

Wakefield, E. G.: Intestinal obstruction produced by mesenteric bands in association with failure of intestinal rotation, 47
Wallis, A. E.: Chronic thyroiditis; comparative analysis of 100 cases, 545
Warren, S.: Fibrosarcoma of soft parts with reference to recurrence and metastasis, 425
Water, hydrodynamics of relief of distention in gastro-intestinal tract by suction applied to inlying catheters, 995
Waugh, J. M.: Effect of fat introduced into jejunum by fistula on motility and emptying time of stomach, 451

Weatherford, H. L.: Rôle of reticulo-endothelial system in deposition of colloidal and particulate matter in articular cavities, 68

Weiss, C.: Experimental pulmonary abscess; transmission of disease to dogs by bronchial route, 649

Witherspoon, J. T.: Roentgen irradiation of ovaries as supplement to surgical and radium therapy for mammary cancer, 554

Woodhall, B.: Acute cerebral injuries; analysis of temperature, pulse and respiration curves, 560

Woodhall, B.—Continued
Cranial venous sinuses; correlation between skull markings and roentgenograms of occipital bone, 867
Variations of cranial venous sinuses in region of torcular Herophili, 297

Wounds, problem of wound healing; effect of local agents, 493

Wrist, movements of wrist joint, 178

Zimmerman, I. M.: Effect of acetylcholine and of physostigmine on gastro-intestinal motility; observations of normal animals and of animals with experimental peritonitis, 187

MEDICAL LIBRARY

DEC 28 1936

VOLUME 33 NUMBER 6

ARCHIVES OF SURGERY

EDITORIAL BOARD

DEAN LEWIS, Baltimore

EVARTS A. GRAHAM, St. Louis — WALLACE I. TERRY, San Francisco

ALTON OCHSNER, New Orleans — WILLIAM DARRACH, New York

WALTMAN WALTERS, Rochester, Minn.

DECEMBER 1936

PUBLISHED MONTHLY BY AMERICAN MEDICAL ASSOCIATION, 535 NORTH DEARBORN STREET, CHICAGO, ILLINOIS. ANNUAL SUBSCRIPTION, $8.00

Entered as Second-Class Matter, July 10, 1925, at the Postoffice at Chicago, Illinois, Under the Act of March 3, 1879.

COPYRIGHT, 1936, BY AMERICAN MEDICAL ASSOCIATION

THE ARCHIVES OF SURGERY is published by the American Medical Association for the advancement of surgery and as a medium of publication for research, clinical observations and experimental work in surgery.

Manuscripts for publication, books for review and correspondence relating to the editorial management should be sent to Dr. Dean Lewis, Editor-in-Chief, Johns Hopkins Hospital, Baltimore, Md., or to any other member of the Editorial Board. Communications regarding subscriptions, reprints, etc., should be addressed, ARCHIVES OF SURGERY, American Medical Association, 535 North Dearborn Street, Chicago.

Articles are accepted for publication on condition that they are contributed solely to the ARCHIVES OF SURGERY. Manuscripts must be typewritten, preferably double spaced, and the original copy should be submitted. Zinc etchings and halftones of illustrations will be supplied by the Association when the original illustrations warrant.

Footnotes and bibliographies should conform to the style of the Quarterly Cumulative Index Medicus, published by the American Medical Association. This requires, in order given: name of author, title of article and name of periodical, with volume, page, month — day of month if weekly — and year.

Matter appearing in the ARCHIVES OF SURGERY is covered by copyright, but, as a rule, no objection will be made to its reproduction in reputable medical journals, if proper credit is given. However, the reproduction for commercial purposes of articles appearing in the ARCHIVES OF SURGERY or in any of the other publications issued by the Association will not be permitted.

Authors will receive one hundred reprints free; additional reprints may be obtained at cost.

The ARCHIVES OF SURGERY is issued monthly. The domestic annual subscription price (two volumes) is $8.00; Canadian, $8.40; foreign, $9.00, including postage. Single copies, 85 cents.

Checks, etc., should be made payable to the AMERICAN MEDICAL ASSOCIATION.

OTHER PERIODICAL PUBLICATIONS

of the American Medical Association

THE JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION—Weekly. Covers all the medical sciences and matters of general medical interest. Illustrated. Annual subscription price (two volumes): Domestic, $7.00; Canadian, $8.50; foreign, $11.00. Single copies, 25 cents.

ARCHIVES OF INTERNAL MEDICINE—Monthly. Devoted to the publication of advanced, original clinical and laboratory investigations in internal medicine. Illustrated. Annual subscription price (two volumes): Domestic, $5.00; Canadian, $5.40; foreign, $6.00. Single copies, 75 cents.

AMERICAN JOURNAL OF DISEASES OF CHILDREN—Monthly. Presents pediatrics as a medical science and as a social problem. It includes carefully prepared collective abstracts based on recent pediatric literature, abstracts from foreign and domestic literature, book reviews, society transactions, etc. Illustrated. Annual subscription price (two volumes): Domestic, $8.00; Canadian, $8.40; foreign, $9.50. Single copies, 85 cents.

ARCHIVES OF NEUROLOGY AND PSYCHIATRY—Monthly. A medium for the presentation of original articles on nervous and mental diseases, with abstracts from foreign and domestic literature, book reviews, society transactions, etc. Illustrated. Annual subscription price (two volumes): Domestic, $8.00; Canadian, $8.40; foreign, $9.50. Single copies, 85 cents.

ARCHIVES OF DERMATOLOGY AND SYPHILOLOGY—Monthly. Devoted to advancing the knowledge of and progress in cutaneous diseases and syphilis. Publishes original contributions and full abstracts of the literature on these two subjects, transactions of the important dermatologic societies, book reviews, etc. Illustrated. Annual subscription price (two volumes): Domestic, $8.00; Canadian, $8.40; foreign, $9.00. Single copies, 85 cents.

ARCHIVES OF OTOLARYNGOLOGY—Monthly. A medium for the presentation of original articles on diseases of the ear, nose and throat, with abstracts from foreign and domestic literature, book reviews, the transactions of special societies, etc. Illustrated. Annual subscription price (two volumes): Domestic, $6.00; Canadian, $6.40; foreign, $7.00. Single copies, 75 cents.

ARCHIVES OF PATHOLOGY—Monthly. A periodical devoted to the publication of original contributions in the field of pathology, with abstracts from foreign and domestic literature, book reviews, the transactions of special societies, etc. Illustrated. Annual subscription price (two volumes): Domestic, $6.00; Canadian, $6.40; foreign, $7.00. Single copies, 75 cents.

ARCHIVES OF OPHTHALMOLOGY—Monthly. Includes original articles on diseases of the eye, abstracts from foreign and domestic literature, book reviews, transactions of special societies, etc. Illustrated. Annual subscription price (two volumes): Domestic, $8.00; Canadian, $8.40; foreign, $9.00. Single copies, 85 cents.

QUARTERLY CUMULATIVE INDEX MEDICUS—Quarterly. A complete subject and author index to the worth-while current medical literature of the world. Issued four times a year. Second and fourth volumes bound for permanent reference. Subscription price, calendar year: Domestic, $12.00; Canadian, $14.00; foreign, $14.00.

AMERICAN MEDICAL ASSOCIATION

535 North Dearborn St. CHICAGO

CONTENTS

PAGE

Differential Analysis of Bile Acids in Human Gallbladder Bile. Ralph Colp, M.D., and Henry Doubilet, M.D., New York 913

Ossification: The Influence of the Mineral Constituents of Bone. J. Dewey Bisgard, M.D., Omaha 926

A Plan for the Treatment of Cancer with Small Quantities of Radium. George T. Pack, M.D., New York 940

The Hydrodynamics of the Relief of Distention in the Gastro-Intestinal Tract by Suction Applied to Inlying Catheters. John Randolph Paine, M.D., Minneapolis. 995

Hernia into the Umbilical Cord and Related Anomalies. L. Albert Thunig, M.D., Brooklyn 1021

Quantitative Studies on Congenital Clefts of the Lip. William T. Peyton, M.D., and Harry P. Ritchie, M.D., Minneapolis 1046

Unusual Cartilaginous Tumor Formation of the Skeleton. Ernst Freund, M.D., Venice, Fla. 1054

A Review of Urologic Surgery (To be Concluded). Albert J. Scholl, M.D., Los Angeles; Frank Hinman, M.D., San Francisco; Alexander von Lichtenberg, M.D., Berlin, Germany; Alexander B. Hepler, M.D., Seattle; Robert Gutierrez, M.D., New York; Gershom J. Thompson, M.D., Rochester, Minn.; James T. Priestley, M.D., Rochester, Minn., and Vincent J. O'Conor, M.D., Chicago 1078

General Index 1117